SEPTEMBER, 1952

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

CONVENTION NUMBER

Program, 17th Annual Convention and Course in Postgraduate Gastroenterology

Pages I-XXIV

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Seventeenth Annual Convention

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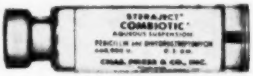

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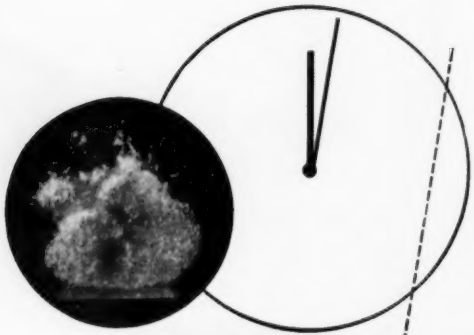

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 19 SEPTEMBER, 1952 NUMBER 9

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CONTENTS

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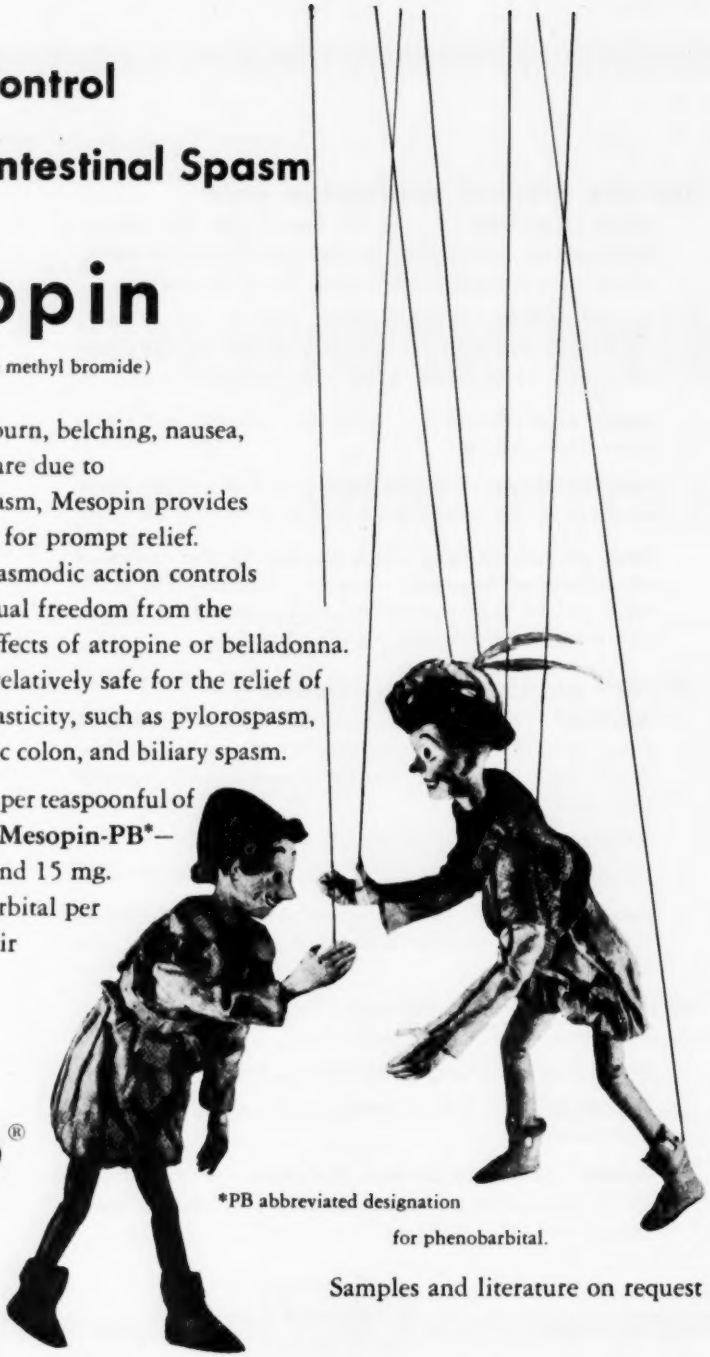

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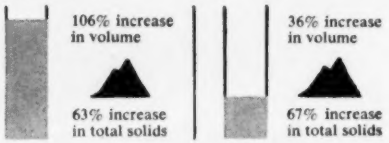

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The Review of Gastroenterology

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Volume 19 SEPTEMBER, 1952 Number 9

MALIGNANCY OF THE DUODENUM*

EARL J. HALLIGAN, M.D., F.A.C.S., F.I.C.S.
LOUIS L. PERKEL, M.D., F.A.C.P.
J. KENNETH CATLAW, M.D., F.I.C.S.
and
LEONARD TROAST, M.D.
Jersey City, N. J.

Progress in the surgical treatment of malignant lesions of the duodenum, pancreas, ampullary and papillary region make it necessary for the gastroenterologist to strive for earlier diagnosis of these lesions.

Malignancy of the duodenum is rare. Approximately three per cent of all intestinal carcinomas occur in the small intestine and from sixteen[1, 17] to forty-five per cent of these occur in the duodenum. Hoffman and Pack[2] reported .033 per cent in over 176,000 autopsies which illustrates the infrequency of this lesion. However, Dixon et al[4] bringing the figures of Lieber, Stewart and Lund[5], Stewart and Lieber[6] and Berger and Koppelman[7] and their own cases in 1946, stated that 718 cases were reported of which 433 were acceptable and, considering the fact many cases are unreported, the lesion may not be quite as infrequent as the textbooks state. Sarcoma is really rare, Brill[8] found one sarcoma of the duodenum in 17,000 cases. Raiford[9] in his analysis of 986 gastrointestinal neoplasms did not report a single case of sarcoma. Prey, Foster and Dennis[11] reported sixty-one cases and one of their own up to 1935.

Lymphosarcoma is the most common, then spindle cell or fibrosarcoma, myosarcoma, melanosarcoma and myxosarcoma. Only sixteen cases of leiomyosarcoma have been reported up to April 1951 (Swartz and Eckman)[12-16].

Carcinoma of the duodenum is usually classified according to the position in reference to the papilla of Vater or ampulla. Therefore they are supra-ampullary or supra-papillary, peri-papillary or peri-ampullary and infra-papillary. Carcinoma may arise from:

*Presented before the Course in Postgraduate Gastroenterology of the National Gastroenterological Association, Chicago, Ill., 20, 21, 22 September 1951.
From the Services of St. Francis Hospital and Jersey City Medical Center.

1) the epithelium lining the true ampulla,

2) the lower end of the common duct,

3) the duct of Wirsung or Santorini,

4) the duodenal mucosa covering the papilla,

5) Brunner's glands,

6) the aberrent pancreatic tissue which is found most often in duodenal diverticula,

7) the duodenal mucosa.

In reviewing the literature it is apparent that forty-five to sixty-five per cent of all carcinomas occur in the peri-papillary portion and twelve to twenty-one per cent in the infra-papillary portion, the rest in the supra-papillary portion. However, many of these tumors arise either in the papilla or ampulla and when these are excluded, the instance of primary carcinoma is nearly equal in all three portions.

Carcinoma of the stomach involving the duodenum is infrequent and usually occurs in only advanced cases. Apparently the reason for this is:—(1) Scarcity of communication between the lymph nodes of the stomach and duodenum. (2) The upward flow of lymph from the duodenum and stomach, or (3) The obliteration of tissue spaces by spasmodic contraction forming a mechanical obstruction to the advance of the malignancy(?).

If carcinoma spreads it is usually via the muscle or subserosal lymphatics, rarely by extension along the mucosa or the submucosa. In contrast to this, submucosal spread into the esophagus is not uncommon.

Carcinoma arising from Brunner's glands apparently are questionable. Robertson[19] observed only two cases in which proliferation in these glands suggested malignancy.

Carcinoma may be of the constricting or stenosing, polypoid or infiltrative type. Colloid carcinoma also has been reported. Polypoid lesions are twice as frequent as ulcerative lesions according to the literature, however, in only one case of ours was the lesion polypoid.

Sarcoma may go on to degeneration, abscess formation with perforation and fistula formation.

Many theories have been advanced both as to the reason for apparent immunity of the duodenum to carcinoma, and against it, because nearly fifty per cent of the malignancies of the small bowel occur here. Hurst[20] states that malignancy is rare due to lack of mechanical irritation because there is no segmentation. The type of peristalsis and the contents of the duodenum are never rubbed against mucosa. In contrast to this fixation of the parietal wall, the presence of the duodenal flexures and being the most widely dilated portion of the small intestine, is

offered as the reason for the prevalence of carcinoma in contrast to the small intestine where there are no fixed flexures, no abrupt bends and the contents are fluid and alkaline[21]. The infrequency of carcinoma of the duodenum is truly remarkable as Dixon[4] states, in an area which is subject to chronic irritation, actually a retort which is constantly charged with acids, alkalis, enzymes, bile salts, cholesterol and the foods we eat and drink.

Proof that the contents are irritating is shown by the presence of ulcer, 99.2 per cent of all duodenal ulcer occurring in the first portion, but here carcinoma is rare[22]. Again, the erosive properties of duodenal contents is seen when duodenal fistula occurs, with its resulting skin irritation.

It is possible that carcinoma may occur from malignant degeneration in an ulcer. In the case reported by one of us[23], five years have elapsed from the onset of the symptoms and three years from roentgen evidence of an ulcer of the cap,

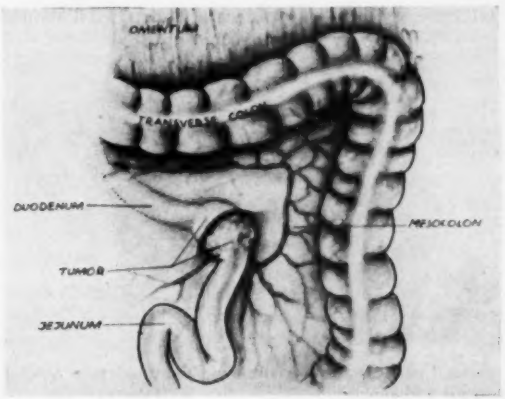

Fig. 1—Malignancy in the distal end of the duodenum is shown. Mesentery has been retracted back for illustrative purposes. Resection of the duodenum for malignancy from 2 cm. below the papilla of Vater down.

until he was operated upon. However, in the cases reported, it is possible as in Jefferson's[24] case and three cases of Dixon et al[4] that malignant degeneration may take place. But it would certainly be an infinitesimal percentage of cases of duodenal ulcer. The age varies from twenty-seven to seventy-four years. The average age — betweeen fifty and sixty years. Males are affected two to three times as often as women, however, in our series it was three to one.

In this series, one occurred in the first portion of the duodenum, one in the second portion and eight in the third portion. Ruling out the case in the second portion as being peri-papillary and one of perforation of the duodenum that may have been perforation from without, we have eight cases of true malignancy of the duodenum.

In the past an effort was made to correlate the symptomatology with the location of the lesion in the duodenum, however, many of these cases were terminal and it was only after death that this was done. Terminal symptoms are of no value if one is to try and relieve or cure these patients. A diagnosis must be made early and the only positive information that will lead us to early diagnosis are the x-ray findings. The symptoms we found to indicate the possibility of this lesion are:

1. Symptoms of obstruction – either of the duodenum or biliary and pancreatic ducts.
2. Loss of blood either acute or chronic.
3. Pain.

Other symptoms and signs may be present, in order of frequency they are: 1) Loss of weight, usually about ten pounds, 2) weakness and lethargy, 3) fatigue, 4) nausea, bloating and belching, 5) anorexia, 6) a palpable mass. The latter occurs in about sixteen to twenty-two per cent and is least common in the infra-

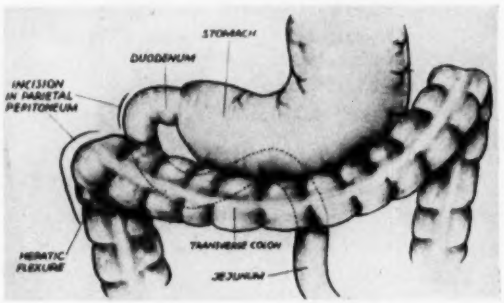

Fig. 2–Incisions in parietal peritoneum for mobilizing the duodenum medially and the hepatic flexure downward and inward.

papillary region. The symptoms are usually present from six to twelve months, although in a case reported by one of us, the symptoms were present for five years and Dixon's[4] two cases giving a history of six years' duration.

Obstruction of the duodenum is usually due to either an encircling lesion causing stenosis, or a polypoid lesion obstructing the lumen. One may have no pain even with a complete obstruction, on the other hand, cramp-like pains of great severity may come on early. Vague epigastric fullness, bloating and anorexia due to incomplete obstruction may be present. As the obstruction becomes more complete, pain and discomfort is apt to increase, vomiting of the retention type is apt to occur. Bile will be present if the lesion is in the third part, but is usually absent if the lesion is in the first part. In lesions of the second portion, bile may or may not be present.

Succussion may be elicited because of the dilatation of the stomach and duo-

denum with retention of their secretions. In one case, (M. McN.) we had complete obstruction with no pain, only severe vomiting.

Cases with marked obstruction show dehydration and electrolyte imbalance with a lowering of the chlorides and sodium, and a rise in the blood urea and nonprotein nitrogen content and carbon dioxide combining power.

Blood loss may be either acute or chronic. In four cases cited below, three of carcinoma and one leiomyosarcoma, massive hemorrhage with its characteristic picture was the predominating symptom.

E. D. was thought to have duodenal ulcer. The irregular outline of the duodenal cap seemed to corroborate that.

J. C. had a duodenal ulcer plus a malignancy of the third portion, and consequently was misinterpreted for duodenal ulcer.

R. M. had been operated upon one and one-half years before for carcinoma of the uterus and her anemia was thought to be due to metastasis until massive hemorrhage occurred.

R. F. had symptoms resembling duodenal ulcer. Her true state of affairs was not recognized until a second massive hemorrhage necessitated an emergency exploration.

Chronic blood loss is apt to occur in all cases due to ulceration or sloughing of the lesion. While gross blood loss may not be present, occult blood is usually found in the stools. These patients may merely present signs of a chronic anemia such as pallor, weakness, fatigue, palpitation and edema of the ankles with no other signs. In fact, it may be mistaken for pernicious anemia, however, the anemia is hypochromic and microcytic.

Obstruction of the biliary and pancreatic ducts may occur early if the carcinoma of the duodenum encroaches upon the papilla of Vater. The location of the obstruction of the biliary tract depends to some extent on the segment of the duodenum involved by the neoplasm. In cases near the pyloric orifice the hepatic ducts are apt to be obstructed and those around the ampulla or below it may involve the lower end of the common duct.

It is very difficult to differentiate carcinoma of the duodenum from carcinoma of the pancreas, bile ducts or papilla of Vater, or even from extrinsic pressure.

Intermittent jaundice may suggest a duodenal carcinoma, because malignancy of the ampulla may ulcerate or slough, causing a variation in the degree of jaundice, or the jaundice may become persistent, more intense and unvarying, due to the involvement of the common duct. Obstructive jaundice of course always has to be differentiated from stone and stricture. The presence of occult blood and diarrhea with jaundice may suggest carcinoma in the second portion

of the duodenum but will not indicate whether it arises from the ampulla, etc., or the duodenum. This of course is academic because if the diagnosis is made of either, the treatment is the same.

Pain is a variable factor in the malignancy of the duodenum. It may be completely absent or it may resemble that of ulcer, coming on from one to four hours after eating and may be relieved by food, vomiting or bicarbonate of soda. It may come on suddenly and may be worse at night, however, it never has the typical pain food ease cycle, for a long time. It may apparently react favorably to an ulcer regime for a few days and then be absolutely refactory to it.

With increasing obstruction, pain is apt to be cramp-like, is usually located in the epigastrium or right upper quadrant. In some patients the pain is persistent and steady and radiates to the back, which usually indicates penetration in the

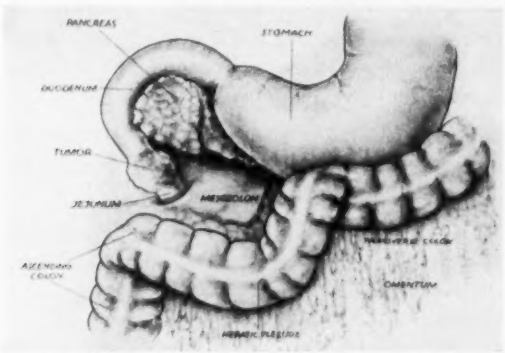

Fig. 3—Hepatic flexure mobilized downward and inwards; duodenum with tumor mobilized upward above mesentery.

pancreas or possible involvement of the nerve plexus in the region of the superior mesenteric artery.

Early loss of appetite is not too common. Diarrhea, when typical, is apt to indicate involvement of the ampulla of Vater, with obstruction of the pancreatic duct. This occurs in thirty-five per cent of the cases of carcinoma of the papilla[25].

Physical examination may not be noteworthy. If the ducts are obstructed a palpable gallbladder may be present. A mass may be palpable in sixteen to twenty-two per cent. Intestinal distention is not present as a rule. The abdomen is usually flat. In late cases with marked obstruction of the duodenum with dilatation of the stomach, peristaltic waves may be present.

The late development of jaundice is consistent with the observations made at autopsy in that obstruction to the extrahepatic biliary passage occurs relatively late, from extension and metastasis to the pancreas, surrounding tissues and regional lymph nodes and exceptionally in part, from the pressure of a large

primary cancer. Of interest in this connection is the statement by Rivers and Thiessen[33] that the appearance of icterus with obstructive lesions of the infrapapillary portion of the duodenum is an almost certain indication of malignancy. Terminal jaundice occurs in the majority of cases.

Laboratory Data:—Most of the laboratory data are not particularly helpful in the diagnosis of malignancy of the duodenum; but they are particularly helpful as a basis for pre- and postoperative treatment.

Complete blood studies are necessary. Diagnostically the various blood studies are in direct relationship to the completeness of the obstruction in the duodenum, biliary tract, or indicate the anemia, whether acute or chronic, from loss due to ulceration or/and sloughing. In the complete obstruction with dehydration, loss of chlorides, sodium potassium and calcium, and a rise of the carbon dioxide, urea and nonprotein nitrogen, etc., is noted.

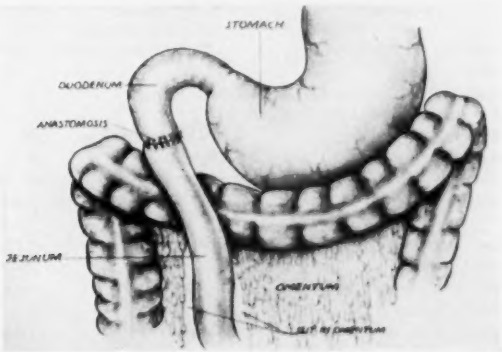

Fig. 4—Shows anastomosis in front of the colon. Anastomosis may be either end-to-end or side-to-side.

With biliary obstruction one has the increased serum bilirubin, decreased prothrombin, absence of urobilinogen in urine, etc., varying with the completeness of the obstruction.

Duodenal aspiration or aspiration of the duodenal contents for bile, cholesterin crystals, calcium bilirubin, white blood cells and epithelial cells is valuable to differentiate from obstruction due to calculus. The staining of epithelial cells by the Papanicolaou method, may really give us some very definite information, if positive.

X-ray examination:—X-ray is the most important factor in the diagnosis of the duodenum. If the gastroenterologist would only keep it in mind at all times and even though he finds a lesion in the stomach or duodenal cap, if he will follow through and carefully observe the rest of the duodenum, earlier diagnoses are possible.

Weber and Kirklin[26] reported seventeen cases, of which the existence of a lesion and its site was made in all but two cases, although the exact diagnosis was only made in nine.

Shallow et al[27] report two cases diagnosed correctly by Dr. Paul Swenson. Usually diagnosis is given as a lesion, a filling defect, polypoid lesion or obstruction of the duodenum. In our own ten cases the diagnosis of duodenal ulcer was made in one. In three, no evidence of any duodenal pathology, and six cases, the lesion was diagnosed correctly by x-ray.

The differential diagnosis is frequently difficult. The lesion in the first portion of the duodenum often being misconstrued as a gastric neoplasm or an old duodenal ulcer with obstruction.

TABLE I

Name	Location	Symptoms	Operative Procedure
1. R. M.	Carcinoma of duodenum, third portion	Massive hemorrhage	Radical pancreatico-duodenectomy
2. G. C.	Carcinoma of duodenum, third portion, plus duodenal ulcer	Bleeding	Gastroenterostomy
3. E. McH.	Carcinoma of duodenum, third portion	Pain, weight loss, vomiting	Resection of duodenum end-to-end anastomosis
4. E. D.	Carcinoma of duodenum, first portion	Bleeding	Resection of stomach including first portion of duodenum
5. R. F.	Leiomyosarcoma of duodenum, third portion	Bleeding	Resection of duodenum end-to-end anastomosis
6. M. C.	Carcinoma of duodenum, third portion	Obstruction	Duodenojejunostomy
7. M. McN.	Carcinoma of duodenum, third portion	Vomiting	Gastroenterostomy
8. D. DeV.	Carcinoma of duodenum, second portion	Obstruction	Gastroenterostomy
9. H. K.	Peri-papillary carcinoma	Jaundiced	Radical pancreatico-duodenectomy
10. M. T.	Perforation of duodenum, third portion	Pain, weight loss, inferior vena caval obstructive syndrome	Found at autopsy

Tumors of the pancreas, common duct, malignancy of the hepatic flexure of the colon and retroperitoneal lymph nodes, all may show x-ray signs similar to malignancy of the duodenum[28].

It is sometimes difficult to accurately localize the obstruction because of the extreme irritability at the site of the lesion. However, an obstruction in the duodenum should be considered malignant until proven otherwise.

Preoperative Treatment:—For the pre- and postoperative studies a complete count hematocrit, blood typing, blood volume, the blood level of sodium potassium, calcium and chlorides, carbon dioxide, serum proteins, prothrombin time

with serum bilirubin determinations are necessary to determine the various deficiencies so they can be corrected preoperatively, and this correction maintained during the postoperative period. All deficiencies must be corrected. Parenteral administration of water and electrolytes, i.e. sodium chlorides, potassium chloride and perhaps calcium (where tetany is present) must be administered to correct these mineral deficiencies. Blood transfusions will correct anemia and hypoproteinemia. Avitaminosis, particularly B, C and K is eliminated by the administration of these vitamins.

Liver reserves, which usually are at a low level, may be brought up to normal by the administration of carbohydrates and protein, particularly glucose given parenterally. Dilatation of the stomach can be reduced by repeated lavage and continuous suction.

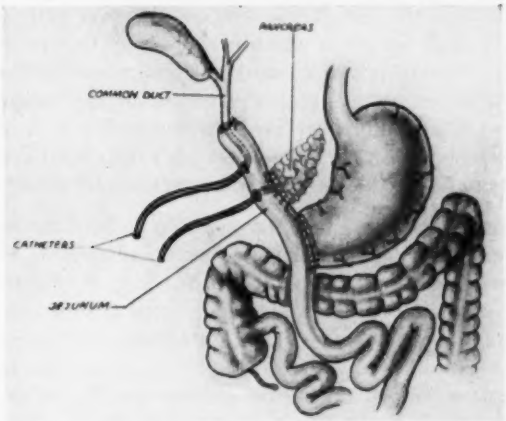

Fig. 5—Shows our usual method of anastomosis. Many variations of the types of anastomosis may be made.
Radical pancreatic duodenectomy with partial gastrectomy, end-to-end anastomosis of common duct to jejunum, end-to-side anastomosis of pancreatic duct to jejunum. Both of these anastomoses are above the end-to-side anastomosis of the stomach to the jejunum. The anastomosis may be either ante- or retrocolic. Catheters are used as splints over which the anastomoses are made and also to prevent the development of biliary or pancreatic fistulae.

Any operation, to be of value in malignancy of the duodenum, must be sufficiently radical to fulfill the concepts of cancer surgery. The mortality must be reasonable, with as little physiological disturbance as possible, so as to be compatible with comfortable living.

Procedures:—1. Local resection of the tumor and a portion of the duodenal wall,

2. Segmental resection of the duodenum with or without a portion of the head of the pancreas or stomach,

3. Radical pancreaticoduodenectomy,

4. Palliative operations, such as gastroenterostomy, duodenojejunostomy, etc.

Criteria of Operability:—Criteria for nonresectability is spread beyond the pancreatic capsule into the lymph glands retroperitoneally, or involvement of the portal vein. Involvement of the superior mesenteric vessels renders the case completely hopeless.

Operation:—Radical pancreaticoduodenectomy is the operation of choice. Radical pancreaticoduodenectomy includes duodenectomy, partial pancreatectomy with the anastomosis of the duct of Wirsung to the jejunum, partial gastrectomy, partial choledochectomy, choledochojejunostomy.

Whipple[34, 35, 39] Trimble et al[36], Orr[37], Waugh and Clagett[32], Brunschwig[38] and Parsons[30], all favor the one stage operation. However, sixty per cent of Cattell's[31] were a two stage operation which enables them to extend the operability to those of long standing jaundice, marked enlargement of the liver and the poor surgical risks for surgery. In stage operations, cholecystojejunostomy is usually done first, but if the gallbladder has been removed or is unsuitable for anastomosis, choledochostomy is done. The latter adds considerable difficulty to second stage operation. Even with this disadvantage, Cattell[31] thinks it is wise.

In doing stage operations, we no longer ligate and cut the common duct because of the danger of the ligature cutting through and creating a biliary fistula or causing a bile peritonitis, and again, in the second stage it is better to implant the distal end of the common duct into the jejunum even though a cholecystojejunostomy has been done. If the common duct is left without drainage, stones may form and be a source of future trouble. Pancreatic fistula, which was fairly common in the early days of pancreaticoduodenectomy, is now uncommon and may be avoided by the use of a tube or catheter as a splint and for drainage; of course accurate anastomosis of the pancreatic duct and jejunum should be done.

When the gallbladder is used as in the first stage of the radical operation, at the second stage the common duct should also be anastomosed to prevent stasis and the formation of stones.

Many types of anastomosis are used. Cattell and Pyrtek[31] at the Lahey Clinic prefer antecolic anastomosis. Waugh and Clagett[32] of the Mayo Clinic favor a postcolic antiperistalic gastroenterostomy.

Radical operation is now technically feasible. The mortality is gradually being reduced to a reasonable level, fourteen and one-half per cent to twenty per cent. The physiological functions are not disturbed so as to interfere with comfortable living.

Pancreaticoduodenectomy offers an improved outlook for an increased number of five-year survivals in carcinoma of the ampulla and duodenum, depending on early diagnosis.

Carcinoma of the ampulla may be diagnosed earlier because signs of obstruction of the biliary tract occur early. While it is not germane to this paper to discuss carcinoma of the ampulla and papilla, because of the difficulty in differentiating them from carcinoma of the duodenum, it is only of academic importance to separate them in the discussion of their treatment which is the same in both instances.

Many other types of anastomosis are used. We favor a one stage operation with end-to-end antecolic anastomosis of the distal end of the jejunum to the common duct, below this an end-to-side anastomosis of the pancreatic duct to the jejunum. The stomach is anastomosed end-to-side to the jejunum, well below the duct anastomosis. Catheters are inserted through the anastomosis of the common duct and pancreatic duct anastomosis to the jejunum, brought out through the jejunal wall below the anastomosis, then through the abdominal wall. This helps

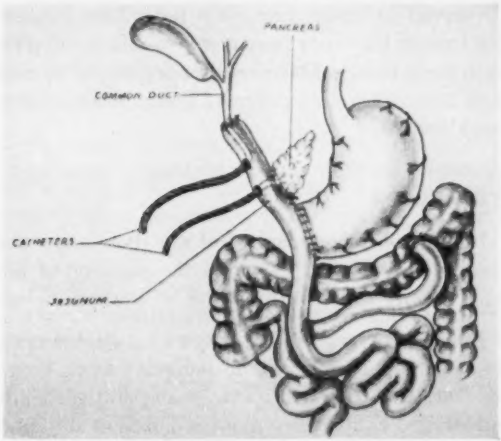

Fig. 6–When the malignancy is nearer the ampulla or when the mesentery is unusually short, this modification is used.

to eliminate the possibility of leakage and fistula formation, (particularly pancreatic fistula). If the mesentery of the jejunum happens to be short, one can transect the jejunum, using the distal portion for the anastomosis and the proximal end is anastomosed to the side of the jejunum below the gastrojejunostomy.

Again, if the mesentery is short a retrocolic end-to-side gastrojejunostomy with implantations of the common duct and pancreatic duct into the loop above the gastrojejunostomy[31] and an enteroanastomosis below the implantations of the ducts is done.

Radical pancreaticoduodenectomy with resection and re-anastomosis of the superior mesenteric vein has been done. The superior mesenteric artery or vein can be clamped off for two hours in dogs, ninety-five minutes in Moore et al's

case[43]. The result was not good, possibly a growth less malignant might be favorably treated.

Other alternatives instead of end-to-end anastomosis of the mesenteric artery and vein are: anastomosis of artery and vein to the aorta and vena cava respectively, transplants of either auto grafts or homo grafts of veins and arteries can be considered, also, end-to-side anastomosis to the aorta and portal vein.

A late complication, without symptoms, is the occurrence of marginal ulcer. Child[41] reporting two cases found at autopsy, one definitely a marginal ulcer, the other was suspected of having a marginal ulcer, one and one-half years after operation, but no evidence was found at autopsy four years later. This raised the question: should vagotomy be done in these cases? Probably not, but further studies are necessary to evaluate this problem.

Segmental resection of the duodenum with or without resection of the pancreas, is usually reserved for those cases that have little local involvement and are poor risks, even though they may have complete obstruction and/or metastasis to the superior mesenteric vessels. One may do a segmental resection to relieve an obstruction due to a constriction or a polypoid lesion in addition to removal of the site of bleeding and sloughing.

Palliative operations such as gastroenterostomy, duodenojejunostomy, etc., may be done for obstruction.

Prognosis:—The outlook for carcinoma of the duodenum in the literature is very gloomy. Felsen and Wolarsky[29] reported the duration of life in infra-papillary carcinoma without surgery, varies from five to nineteen months.

Bernard and Koppelman[7] reported twenty-two collected cases of infra-papillary carcinoma of the duodenum in which palliative operations or explorations were done. There were eighteen immediate postoperative deaths, a ninety per cent mortality, and all died within three months. Dixon et al[4] report twenty gastroenterostomies with an average survival period of twenty-one months; four lived seven, six, three, and two and one-half years.

Shallow and associates[27] collected fifteen cases of infra-papillary carcinoma of the duodenum of which seven lived over a year; two lived three years or more.

Of the patients of Dixon's[4] cases only two were alive two years after operation of infra-papillary carcinoma.

Parsons[30] reports four cases of cancer of the duodenum or ampullary region without spread. One lived four years; one, three years and two, under one year. Four cases with extension (one lived two and one-half years; one, twenty-eight months; one, twenty-seven months; one, fourteen months).

Cattell and Pyrtek[31] report twenty cases of carcinoma of the ampulla; carcinoma of the head of the pancreas, thirty cases; carcinoma of the duodenum, four

cases; carcinoma of the common duct, two cases. Which represented an operability of thirty-four per cent.

Mortality:—Operative mortality following pancreaticoduodenal resection has varied in reported series from eleven to forty-five per cent. Cattell and Pyrtek[31] report a mortality of fourteen and three-tenths per cent, in that, we have a five per cent mortality for four cases of carcinoma of the duodenum and a two per cent of carcinoma of the common duct. Two cases of carcinoma of the duodenum lived two years and eight months respectively, with carcinoma of the ampulla, twenty-five per cent lived five years, and fifty per cent lived three years.

Extension into the local lymph nodes appears early but there seems to be a long period before it spreads to the liver, lungs and bones. Waugh and Claggett[32] report a twenty per cent mortality.

Conclusions

True malignancy of the duodenum is rare but it should always be kept in mind by gastroenterologists.

Early diagnosis means an increase in the number of five-year survivals.

Although the reports in the literature offer a gloomy outlook, radical pancreaticoduodenectomy offers an improved chance in the cure of carcinoma of the duodenum.

It is true we are only discussing malignancy of the duodenum, but it is only of academic importance to separate peri-papillary carcinoma from carcinoma of the duodenum. The treatment is the same.

Ten cases of malignancy of the duodenum (one previously reported by one of us) have been studied and the literature reviewed.

1. One case of leiomyosarcoma which will be a subject of a later report,
2. One supra-papillary carcinoma,
3. One peri-papillary carcinoma,
4. Seven infra-papillary carcinomas are reported.

Of these, eight were proven malignancies by histological evidence. Three had segmental resections; two had radical pancreaticoduodenectomy; three had gastroenterostomy and one had duodenojejunostomy. One discovered at autopsy. Nine cases were seen in the last year and one-half, three are still alive and well.

While it is very nice to be able to make a diagnosis of the portion of the duodenum in which the lesion occurs, we agree with Dixon[4], if one recognizes the possibility of the lesion of the pancreas, duodenum or bile ducts early, and follows it up with careful x-ray studies, it is more important.

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Discussion

Dr. Walter Freymann:—I wish to add to Dr. Halligan's excellent presentation a very short comment on the possibility of visualizing the duodenum and part of the jejunum. A Dr. Bendick, chief of radiology in one of the large hospitals in New York, the name of which is not known to me, has lately introduced a technic to fill duodenum and jejunum, beyond the ligament of Treitz, without using intubation. He has the patient drink four to five swallows of heavy barium while being fluoroscoped. A small bottle of soda water is immediately given to the patient, who is then put on the x-ray table in supine Trendelenburg position. This method shows cardia and antrum filled with barium, while the stomach itself is filled with water and floats below the abdominal wall; duodenum and jejunum, – the latter, up to eight inches beyond the ligament of Treitz, can be seen filled with barium. This method has enabled Dr. Bendick to show malignancies and diverticula, which otherwise could not be located or even assumed. I think that this new technic is excellent – it requires no instruments of any kind – and will help in early recognition of abnormalities in duodenum and jejunum, which otherwise might be missed.

Dr. Earl J. Halligan:—Dr. Wangensteen has brought up the question of gastric analysis. Most of us feel that gastric analysis isn't worth much unless it is done routinely. We use the alcohol and/or histamine test and you may find achlorhydria, normal acidity or hyperacidity with a chronic gastric ulcer.

We have had an ulcer at the juxta-esophageal junction which had definite achlorhydria even with the histamine test. We did a total gastrectomy. Serial section showed no evidence of malignancy.

I believe those stomach cases that have chronic cholecystitis associated with them, show that the gastric analysis has not been too profitable, however, when you do have an achlorhydria, you are suspicious, particularly if you have a gastric ulcer. We advise resection. Ten to fourteen per cent of all gastric ulcers are malignant and therefore, we are inclined to do a resection of all gastric ulcers irrespective of the acidity.

I was interested in Dr. Freyman's discussion on the visualizing of the duodenum and upper jejunum. It is most important and should be carried out in all cases, particularly if the gastrointestinal x-ray is unsatisfactory in explaining the symptoms.

Dr. Wangensteen brought up the question of age. That may be important. The age plays no part in our consideration in most cases. Often they are physiologically young, younger than their chronological age. Our oldest case of total gastrectomy was eighty-two. We have had protestations on the part of the practitioners, that a man or woman eighty to ninety years of age shouldn't be operated upon. One of our colleagues felt so strongly about it he looked up the statistics and found at eighty-two years of age the life expectancy was only two years.

We feel it doesn't make any difference how long they live; it is how long they live comfortably which is the more important thing.

If we can do something for these people, no matter what the age, I believe it is worthwhile. We have had many cases between eighty and ninety. We just resected two people seventy years of age for malignancy and did practically a total gastrectomy. One must recognize the fact that they will be mistaken for pernicious anemia, and that there is always a secondary anemia. In resection of both the duodenum and the stomach one may develop a pernicious anemia. The intrinsic factor is present in both stomach and duodenum in the human being. It was thought that total gastrectomy would always be followed by a pernicious or a pernicious-like anemia because it was thought the intrinsic factor was completely removed. However, this was based on dogs, because the intrinsic factor in dogs is in the gastric portion of the stomach rather than the duodenal tube. In the human being we find that intrinsic factor is both in the stomach and duodenum, and one can do a total resection of the stomach or a total duodenectomy with a partial removal of the other organ without getting a pernicious anemia. We have some cases of total gastrectomy going on eight years, with a portion of the duodenum resected for carcinoma and they have had no signs or symptoms of pernicious anemia.

I think we have been fooled to a certain extent in expecting pernicious anemia in every case of this kind. We have had one case of hypertrophic gastritis where hemorrhage was so great and severe we had to do almost a total gastrectomy to control it. In this type of case where bleeding is a dangerous complication we advise emergency gastrectomy.

THE IMPORTANCE OF LYMPH NODES IN GASTROINTESTINAL CARCINOMA*

R. K. GILCHRIST, M.D.

Chicago, Ill.

First I should like to know how many of you do bowel surgery. Thank you. This is mostly for the medical men because I think it is very important for the medical men to know the problems in surgery of cancer of the gastrointestinal tract, and to see that these patients are given their money's worth.

A number of years ago we were much impressed with the fact that we were unable to guess which of our patients would have a long term cure and which ones would have a recurrence shortly after resection of the bowel for cancer. I should like to go through a little of this material to try to give you our idea of how cancer spreads and what it is possible to do and still have not only life but patients who can live comfortably.

We devised a modification for clearing specimens.

(Slide) It was not difficult to get a large number of lymph nodes. We made full scale drawings of each specimen. This is a carcinoma of the rectum, and these little round dots are lymph nodes. It is possible to get nodes as low as a half a low power field at a hundred diameters. I will talk to you about lymph nodes removed from 200 patients who had carcinoma of the colon. These are not consecutive cases, but every patient who entered the hospital and who, we thought, had a chance of cure and who died after surgery or who had an unfavorable lesion is included.

We made full scale drawings of every specimen and the nodes were sectioned individually, and posted on the drawings in India ink.

We averaged over 10,000 nodes. The average number of lymph nodes in carcinoma with abdominoperineal resection is 55, and I don't think anybody realized before that there might be as many as 210 lymph nodes in that area. Sixty-odd per cent of the patients we thought had a chance of cure had metastases in the lymph nodes at the time of operation.

Cancer spreads in three ways: by direct extension, and you who are surgeons know how far it spreads, by looking at it; it spreads through the blood stream, and that is hard to determine even microscopically in the early stage, but somewhere between 10 and 15 per cent of the patients with cancer of the bowel do have blood stream spread.

The work of Coller's group at Ann Arbor, as well as others studying the lymphatic spread of cancer in lesions of the breast, stomach and colon, showed

*Presented before the Course in Postgraduate Gastroenterology of the National Gastroenterological Association, Chicago, Ill., 20, 21, 22 September 1951.

that about two-thirds of all patients who were thought to have a chance of cure had lymph node meastases at the time of surgery if the study was carried out in this way. This spread of cancer through the lymph system had a definite pattern which was predictable and the manner of this spread will be our thesis today

If you take a colored viscid solution, any type of dye, and insert it directly in the lymph channel of an animal, you will find that when injected under low pressure, the solution will go through the node and out of the efferent part of the node without even coloring all the node. In contrast, if you inject a suspension of fine insoluble particles, all of which are less than one micron in diameter, you get an entirely different picture.

You can use 100 cm. of pressure or more, but you will not get any of these particles to go through that node. They will be arrested, and the first few metastases of these insoluble materials will land in the subcapsular spaces, and if a little more is used (and you have to make the preparations transparent to see this) the particles will land in three or four parts of the same node. When the first node is filled, three or four adjacent nodes will also be filled through the short collateral channels. When these are fairly well blocked, you can inject with above 100 cm. of water pressure, and particles will not go through, but the suspension has to go somewhere and it gradually goes in a retrograde manner, and it eventually is routed to a more centrally placed node. In other words, you have here a system of filters that the body has provided which effectually blocks the spread of these particles as well as tumor emboli.

At the turn of the century, Sampson Handley proposed that cancer grew through a lymph channel, through the node and up the efferent node, and so forth. Unfortunately, the prairie fire had spread long before he made his study, on patients dying of cancer of the breast and he had no chance really to tell what happened. In over 10,000 nodes I have here, and almost another 10,000 done by some others which have never been published, and a great many by C ller and his group, and over 3,000 of the breast by Monroe, we have only about a dozen cases where we have lymph channels filled with cancer, where we do not have the nodes central to the lesion involved.

It is an embolic process, not one of permeation or growth in continuity, and that is the thesis. There is a defense. You can tell where the spread is going to be, and anything less than removal of the tumor, and not only the first chain of filters but also the first alternate chain of filters, will give no chance of cure in three-fourths to two-thirds of the patients you see.

(Slide) I want to show some of our material. This is a small node, one less than one low power field in 100 diameters. There are a few cancer cells here and over them the capsule of the node is thick, whereas it is not elsewhere, and that you will see in all of these slides. We do not find cancer breaking through the capsule of the node except when there is heavy metastasis.

This woman had cancer of the breast. I injected the lymphatics after she was asleep. Here is the carbon suspension in one part of the node and the node is almost replaced by cancer. The capsule is thick where there is cancer; in other words, a node which is not completely replaced by cancer will still function and still will arrest additional cancer emboli.

(Slide) Here is a small node which has a lymph channel involved. This is a very minute node. It is fairly heavily involved with cancer, and this patient had many other nodes involved.

What about the patient with local resection? We are in the center of an area where we have surgeons of repute who preach that in cancer of the breast they can do as well with local resection and x-ray as by radical resection, and I am sure they do. I don't think it is true of all of us. I think some of us can do better, but here is one such patient.

This woman was a schoolteacher and an intelligent one. She had a local mastectomy eight years before I saw her. She fell while dressing and scratched her rib three or four inches below the edge of the scar and got an infected wound. She came three weeks later with an enlarged Garotta node back of the pectoralis major muscle. It was the size of a finger. It was inflamed and I said, "we will put warm dressing on it." This was long before the days of chemotherapy. She didn't like it. She said, "No, that is cancer. You get it out."

I said, "I will lift it out."

Here it is. That cancer was lying dormant there in the node for eight years. She had had some radiation, but these are pyknotic cancer cells in scar, and under the influence of inflammation or by happenstance, they began to grow. You will see the appearance of the pyknotic cancer cells, and we will show you other sections from the same node. This is part of the cancer which was buried in scar tissue, and the cells lay for a long time without any trouble.

(Slide) And here is a sheet of cells in the same node. It is almost impossible to tell where they came from. We cleaned out the axilla, and she had four or five other nodes involved which looked about like these. This node, as you see, had finally broken through. She lived eight more years and then had a coronary thrombosis, died of it, and was posted and no cancer could be found.

If that first node had been from a cancer in the gastrointestinal tract, she would have had no chances of cure, as it would not have been palpable when it first began to enlarge, and I am sure that happens repeatedly. In other words, the x-ray only arrests the cancer cells, it does not kill those in the nodes.

Every lymph node has a blood vessel supplying it. If you come over to the Presbyterian Hospital, I will show you some of the cleared specimens, and you can see the vessels even in minute nodes. Here is a node that has its vein packed with cancer cells. I think this is the source of the multiple emboli we get all over

the body; twenty or twenty-five years after a woman has a breast removed for cancer – and we see it, though not so frequently in other lesions – the lesion is dormant as in this one we have shown you – something happens and it finally begins to grow and invades the vein. It is found all over the body and they say, "Look, here, it has been all over all this time." I don't think that is so.

(Slide) This patient had carcinoma of the cecum. It broke through the bowel, and this is the reason you get good results even with large carcinomas of the cecum and with many nodes involved. Here is a large node. It is not hard to do a really, truly radical resection of the mesentery, draining cancers here, and which one of you, as surgeons or medical men, ever heard any surgeon ever admit he did anything less than the most radical operation that ever could be done on any cancer? I never did. There is the most marked difference in the degree and amount of surgery done under the label of "radical surgery" that it is possible to imagine.

We have men who do lots of bowel surgery and who say a resection of the bowel wall 2 centimeters below or above the lesions is sufficient, but I find this case of a man with this annular lesion and I resected the full thickness of the abdominal wall, except the skin. He had one minute node up here, just 5 cm. proximal to the lesion, in an appendices epiploicae, and there was a cancer in it. Had we resected 2, 3, 4, or 4.9 cm. proximal to the tumor, he would have had a local recurrence. There is no reason to resect close to the lesion if you are trying to cure them. Spread to nodes in this same location can be demonstrated by injections in fresh postmortem preparations.

(Slide) We had 19 patients die in the hospital in this group, we got postmortem on 12. Of the 12, 4 had postmortems by the ordinary method used by all pathologists and in no case could we find any cancer with the ordinary postmortem, but of the other 8, I cleared the retroperitoneal tissue from the celiac axis to the bottom of the pelvis. This man had this cancer biopsied one year before, and was told he had a cancer and ought to have his bowel out. It is an anaplastic lesion. So he waited a year and changed doctors, as so many do.

Dr. David did this resection, and he had forty-seven lymph nodes containing metastases. He lived for seven or eight days; had a pulmonary embolus and was dead in five minutes. Here are 165 lymph nodes in the retroperitoneal tissues, each one individually sectioned. One node had cancer metastases. I have a label on it. I can show it. It is No. 116. A half a centimeter wide resection would have cured the man of cancer if he had survived the operation.

(Slide) Here is another one. He had a chronic cough. He wasn't very vigorous, and he had less than the usual resection because the surgeon was a little timorous about his condition. If the inferior mesenteric artery had been resected at the aorta, all of his cancer could have been removed.

(Slide) Another one with node metastases above and laterally. These are a

centimeter out of the field of resection. We have the lateral spread demonstrated here, so the surgeons and pathologists who tell you they have gone back and reviewed 150 specimens, or 200 or 300, and can't find lateral spread are right — of course, they can't. Neither can I on most operative specimens. We didn't get the lateral node here, and that is the weak spot in the surgery of cancer in this region. It is difficult to go out and get the nodes because you are likely to injure the ureters and bladder, and there is apt to be a neurogenic bladder afterwards. But you can get some of them, and if I had more time, I would show you some. I just want to point out when metastases to lateral nodes are not found on the specimens, it doesn't mean they were not present.

(Slide) That patient could have been cured. This man had a coronary ten months before operation, and had an obstruction resection. He had a number of enlarged, involved nodes here. He died after two or three weeks. At the postmortem preparation he had 168 lymph nodes in the specimen. There is only one remaining node which contained cancer. We missed removing all of his cancer by a centimeter.

So, of the patients with node metastases who died and were posted, of whom there were eight, in four we had missed removing all the involved nodes, and in three of the four we could have cured them by a resection of the mesentery that was 1.5 cm. wide of what we did.

Now what should you do?

(Slide) Well, I am going over our results just a little bit. We have 15 tumors of the right colon who had nodes involved. This is the highest incidence of lymph node metastases of any. Fifteen were resected, and while they had large nodes, we thought they had some chance of cure. Three died in the hospital, and one was lost to follow-up. Seven were well five years, which is surprising, only it isn't surprising when we look at the lymphatic metastases.

(Slide) This type of resection is easy and any surgeon who does bowel surgery ought to be able to do this without difficulty. It is not a matter of the amount of bowel, but of the amount of mesentery which is removed.

In my opinion there is no compromise if you are talking about surgery for cure in cancer, and there is a place for palliative surgery which I cannot discuss with you at this time.

(Slide) There is a little different problem when you have a lesion at the hepatic flexure which reaches to this point because there is a double lymph drainage and you may catch it at the right midcolic branch. There is a principle of defense involved here because of defense in depth with the nodes. So what I call the conservative operation — I will not call them radical any more, since every piece of bowel taken out for cancer is called radical in every clinic in the country, and I think we ought to realize that not all patients with tumors in the same tis-

sues need the same operation, but the least you can do for cure is to take out this much bowel, and mesentery, and if it is a penetrating lesion and looks suspicious at all, you need to take the midcolic artery at the lower end of the pancreas, and the ileocolic, which means you have to take out this much bowel, anastomosing the splenic flexure to the ileum. It is still no trouble to put them together, and they will do all right.

(Slide) Now for lesions of the transverse colon. All of this group had the V-shaped obstruction resection. This was in the preantibiotic days. We don't do this any more. Three are alive and well five years out of eight. Those who had no nodes involved had 100 per cent cure. I don't believe there is any argument about it. You go right down and take over the midcolic artery at the inferior edge of the pancreas. You can do a side-to-side or end-to-end.

(Slide) The old V-shaped resection is what has been done in the descending colon, but it is not adequate – certainly our results were not – and the least you can do, I think, is to incise the peritoneum below the ligament of Treitz, and take all aortic fat and nodes off down to the bifurcation. It is easily possible and takes much less time than you think if you have made up your mind to do it. It is no trick to put the ends together.

I have one such I did five years and four months ago. He was working as a Pullman porter, and he had an involved node between the aorta and vena cava, just above the origin of the inferior mesenteric artery. The vessels were cleared of fat and nodes as described, removing the inferior mesenteric artery. Continuity was re-established and he is still well and working. As a final word, there is a place for resection for palliation. It should be discussed separately from resection for cure, but any operation that you do or your surgeon does for cancer of the bowel means you must take out the bowel that contains the cancer. You must not in the lower lesions go less than an inch and a half below them, and the important point is the resection of the mesentery. You ought to get all the first chain of filters and all the first alternates, if possible, and in most cases in abdominal lesions, you can re-establish function, and the mortality will be no greater than the other way.

Discussion

Dr. I. Snapper:—I am certain that everybody must be deeply impressed by the material Dr. Gilchrist has shown us. It is really terrifying that lymph nodes far distant from the primary tumor are so often involved. Since hardly any surgeon does the radical operation for cancer of the colon as is necessary in view of Dr. Gilchrist's finding, it can hardly be explained why so many surgeons imagine that they can obtain very favorable results in colon tumors. I am afraid that the inborn optimism which characterizes the surgeons must have colored their figures with a rosy hue. We certainly must be grateful to Dr. Gilchrist that he has clarified this situation.

I dare to say that this investigation can be compared with the revolutionizing work of Simpson Handley, who forty years ago demonstrated the widespread lymphatic permeation in carcinoma.

Dr. Earl J. Halligan:—The work of Dr. Gilchrist has been really monumental and is really the basis of all radical surgery of the gastrointestinal tract because it has opened up a new field for us. I know that after reading his first publication, I increased the field of operability and removed a lot more than I had done previously. I always remove the right half of the colon, where the results are better, but it was in the left half of the colon that results were poor. We increased the extent of our operability. We removed the whole left half of the colon, and, as Dr. Wangensteen has said, we even now consider total colectomy. Where we have polyps in addition to carcinoma, we do a total colectomy.

My main question is to ask Dr. Gilchrist about the material he uses, the carbon preparation for the injection of these lymphatics, and does he do this intravitally.

We have a project now whereby we are staining the node by injecting with sky blue dye, particularly in carcinoma of the stomach, to see which nodes are involved and which are completely involved, which won't take up the dye and which are partly involved and to indicate the nodes so we can do a very complete resection. You have to wait about fifteen or twenty minutes after you inject the dye so the nodes will be outlined but it is too early to arrive at any conclusions yet. We started the work a short time ago. It is interesting and will give us some idea of the nodes definitely involved and those not involved and give us some idea of the lymphatic drainage in carcinoma of the stomach and also in colonic carcinoma.

We also should like to know more about the spread. Lateral spread is most important. We have had lateral spread in the gut itself for a distance of 13 cm. If one does a radical operation, as advised by Dr. Gilchrist, one must remember the lateral spread as well as mesenteric spread.

There is one more point and that is in carcinoma of the rectum. The smallest lesion I have ever seen was about one-half the size of my small fingernail. It was 10 cm. from the mucocutaneous junction and was picked up by a very astute gastroenterologist who proctoscoped the patient and got a biopsy. It was presented to me on account of the biopsy. Through the damage done by biopsy they could not recognize the lesion when they presented it to me but it was adenocarcinoma definitely, a Grade II. We did an anterior resection on her because we felt that she was the ideal case. Within six months she had recurrence not only in the suture line but also in the pelvis.

We wonder about the views of Dr. Gilchrist on that. We feel that we have eliminated those cases by doing an abdominoperineal resection on all cases with involvement below the peritoneal reflection.

Dr. R. K. Gilchrist:—I think Dr. Wangensteen's "second looks" pose two or three problems. If you do a resection on the basis of the general premise that we have laid out here, you won't have very many metastases in other lymph nodes unless the tumor was adherent to another structure or if it had broken through the serosa of the bowel, in which case you have a primary which now can be seen anywhere in the abdominal cavity, which may again spread to other nodes.

The most common example is the rectal shelf seen in cancer of the stomach. I haven't done "second looks". I suppose we may. We will let him work out this problem.

Have you time for two slides on the breast? It will take one minute.

(Slide) I just want to point out that in the same hospital in Chicago where the same skin incision was used, where every surgeon except one removed the major and minor muscles, that the number of nodes removed, as studied by Dr. Monroe, averaged 16, where the others averaged 45, and this shows that there is no place for compromise.

(Slide) Now, here are the results by the five or six surgeons who did most of the resections. The man who has 16 lymph nodes and who says that he does just as well by the conservative operation which Dr. Popper advocates, and if you will notice the patients with no nodes involved — the little stippled squares — only half of his patients who had no nodes involved were well five years, of course, these form a small series because there is a tremendous lot of work in this — over 3,000 different node sections in this group, but of those who have nodes involved, only one of five was well five years.

The next surgeon averaged 28 nodes, and two-thirds were well five years, and of those with nodes positive, over 40 per cent were well.

The next surgeon, who is here with four lost to follow-up, all having been positive cases and presumably they died, and from there on these surgeons averaged 28.8 up to 46 nodes per specimen, and every one of them had every patient with no nodes involved, known to be alive and free of cancer over five years.

If you look down the line, you will notice as the number of nodes resected increased, the cure rate rose. Of those with over 50 nodes removed per specimen, regardless of which surgeon operated, 55 per cent of those with positive nodes were free of disease over five years, and that is pretty hard to laugh off.

THE PROBLEM OF GASTROINTESTINAL DISTURBANCES ATTRIBUTED TO ALLERGY*

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Nausea, vomiting, disturbed intestinal motility and other symptoms referable to the gastrointestinal tract may be part of the clinical manifestations of many organic or functional conditions. These symptoms, which can occur without any associated lesions involving the digestive system frequently accompany asthmatic attacks. They do not necessarily indicate the presence of gastrointestinal allergy. Symptoms of indigestion are so common and can occur from such a multitude of causes that often it is difficult to determine whether they are the result of direct injury to the gastrointestinal organs or are of reflex or purely psychogenic origin. Although usually gastrointestinal symptoms such as are present during asthmatic attacks are not due to gastrointestinal allergy in the strict sense, it has been established by sound clinical and experimental evidence that allergic reactions can and do occur in the organs of the digestive system. The classic report of Oscar Schloss[1] in 1912 decribes the symptoms and course of acute gastrointestinal allergy.

"The child," he wrote, "took only a few tastes (of soft-boiled egg), cried, and refused more. Almost immediately he began to claw at his mouth and the tongue and buccal tissues swelled." At a later time: "the child ate a few small cakes in the preparation of which egg was used. Within a few moments he began to vomit" and associated allergic symptoms followed rapidly. Schloss[2] experimentally produced diarrhea and watery stools by the injection of a shocking dose of egg white into guinea pigs which previously had been sensitized by feeding large amounts of egg. Ratner[3] also induced retching and vomiting, followed by asthma, by feeding milk to guinea pigs three weeks after sensitization to milk by forced milk feeding.

Acute gastrointestinal allergy need not be necessarily the result of sensitivity to foods. Food allergy and gastrointestinal allergy are by no means synonymous. The acute abdominal distress seen frequently in anaphylactoid purpura is a well recognized example of gastrointestinal allergy in which the causal antigen is more often a drug or some product of microbic infection than a food. When acute gastrointestinal symptoms are caused by an allergic reaction to a food the causal relation usually is recognized by the patient or his family and the offending food avoided. Chronic symptoms are less dramatic, tend to be present more constantly, and when actually caused by food allergy there is no clear cut relation to the ingestion of the offender. For these reasons harmless foods are often suspected and unnecessarily eliminated from the diet. Since an antigen-antibody reaction is essential to the concept of allergy there is no justification for attributing vague

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gastrointestinal symptoms of unknown etiology to allergy unless direct or indirect evidence of such an immunologic reaction can be obtained. Acute symptoms of gastrointestinal allergy occur not infrequently as part of a constitutional reaction to an injected antigen. We recently observed an example of this type of gastrointestinal allergy in a twenty-six year old woman. She had been given her scheduled treatment dose of 400 P.N.U. of ragweed antigen, subsequently remained in the office without symptoms during a twenty minute period of observation and then went shopping. A short time later she felt a sensation of generalized heat and pruritus. Tightness in the chest and severe nausea rapidly followed. Two hours after the injection she had intense cramping abdominal pain together with vomiting. Temporary relief promptly followed hypodermic epinephrine but later that evening there was recurrence of nausea and abdominal pain, urticaria developed and these symptoms continued throughout most of that night. Her gastrointestinal symptoms probably were due to smooth muscle spasm and to urticarial whealing of the gastrointestinal mucosa.

Acute gastrointestinal allergy such as that described usually is transitory and recovery is complete without lasting tissue damage. Sometimes, however, more severe and less transitory reactions occur. Irreversible allergic perivascular lesions involving those tissues or organs which happen to bear the brunt of the shock may then result. Berne[4] has reported such a grave reaction to penicillin given to a 53 year old man for pneumonia. General urticaria developed and was accompanied by purpuric lesions which progressed into subcutaneous hemorrhages. Paralytic ileus with signs of peritonitis and shock followed, and death from pulmonary edema occurred on the fifth day. At necropsy the walls of the duodenum, small intestine and cecum were friable and there were diffuse hemorrhagic areas of necrosis in the mucosa. Arteries and veins of the submucosa showed acute necrotizing angitis. The pathologic lesions, believed due to penicillin hypersensitivity, were essentially limited to the skin and intestinal tract and the case may be regarded as an instance of fatal acute gastrointestinal allergy.

While there is general acceptance of the role of allergy in instances of acute gastrointestinal allergy such as in the cases cited, there is widely divergent opinion concerning the frequency of allergy as a cause of chronic indigestion, diarrhea and a multitude of other nondescript digestive symptoms and complaints. Rowe[5] states ". . . it is my opinion that a large percentage of all symptoms arising in the alimentary tract and abdomen is due to food sensitizations." Cooke[6] on the contrary writes, "my own experience leads me to state the frequency in this way: acute gastrointestinal symptoms, with or without systemic evidences (urticaria, asthma) from allergic lesions reasonably assumed to exist in the tract are unusual but not rare. . . . Cases proven to be allergic, having had persistent or recurring gastrointestinal symptoms that constitute the primary reason for seeking medical advice, are not in my opinion common, and certainly not as common as might be inferred from the literature on allergy." He adds that there are no available data on the frequency of gastrointestinal allergy.

TABLE I

INCIDENCE OF ASTHMA, RHINITIS, URTICARIA, CHRONIC GASTROINTESTINAL SYMPTOMS AND FOOD ALLERGY IN 1,000 CONSECUTIVE PRIVATE PATIENTS

	Asthma		Rhinitis		Urticaria			Gastrointestinal		Food Allergy	Total
Male Age Group	Atopic & Combined	Infective	Atopic & Combined	Infective	Acute	Chronic	Angioedema	Allergic	Not Allergic		
Under 5	27	12	8	7	6	0	5	1	0	9	69
5 to 11	58	7	81	14	6	1	2	4	1	18	110
12 to 19	26	0	46	2	2	0	1	0	0	2	55
20 to 39	43	3	71	14	7	0	2	2	1	16	105
40 to 59	31	8	28	28	4	5	4	0	7	5	90
Over 59	3	8	4	6	2	0	0	0	2	1	29
Female Age Group											
Under 5	8	8	4	7	4	1	3	0	0	9	43
5 to 11	26	6	14	4	3	1	0	0	0	5	57
12 to 19	16	4	21	4	5	1	3	0	0	8	59
20 to 39	192	12	82	33	21	8	10	0	7	15	192
40 to 59	33	15	19	20	14	6	5	0	1	9	135
Over 59	3	4	1	3	2	0	3	0	2	1	26
Total Male	188	38	238	71	27	6	14	7	11	51	458
Total Female	278	49	141	71	76	17	24	0	10	47	512
Total both	466	87	379	142	103	23	38	7	21	98	970*

*Thirty patients were not included because no study was made.

I have reviewed the recorded incidence of symptoms that might be attributable to gastrointestinal allergy in the last one thousand consecutive private patients seen. The general routine of study for these patients included a comprehensive history taken either personally or by my associate, urinalysis, differential blood count, sedimentation rate, Kahn test, tuberculin test, and indicated special laboratory and roentgen examinations. The allergy investigation included cutaneous and intracutaneous tests with the usual food and inhalant allergens. In addition, patients with asthma, perennial rhinitis, atopic dermatitis, digestive complaints or other symptoms possibly attributable to food allergy were further studied by diet trial. For several years in the diagnosis of food allergy in addition to skin tests we have used a provocative diet, modified from that described by Andresen[7]. We have been increasingly convinced of the value of this procedure as an aid in the recognition of true food allergy and in the exclusion of pseudo-food allergy as a cause of symptoms attributed to hypersensitivity[8]. Pertinent selected data from each case record, including age, sex, major diagnoses and demonstrated sensitivities recorded on "Keysort" cards were available for this analysis.

Almost all of the patients included in this series had symptoms which they or the referring physician believed to be attributable to allergy. For this reason one might justifiably expect gastrointestinal allergy to be encountered more frequently than in a group less weighted by allergy. Although 466 of these patients had asthma, 379 had allergic rhinitis, and 126 had acute or chronic urticaria, it was found that chronic gastrointestinal symptoms were recorded for only 28 patients. A diagnosis of gastrointestinal allergy was believed justified in only 7 of these (Table I). This surprisingly low incidence would be somewhat increased if past acute gastrointestinal allergic reactions recorded in the histories of many of these patients and recognized as due to the ingestion of egg, nuts, fish, cottonseed meal, or other similar potent antigens were included. The potential incidence of such acute reactions can be inferred from the tabulation of such sensitivities found in these patients (Table II).

Because food antigens remain in contact with the gastrointestinal mucosa during digestion, one might expect evidences of an allergic reaction with digestive symptoms to occur from relatively slight contact when specific hypersensitivity is present. Such is not the case. Fergen and Campbell[9] found that specific and nonspecific substances caused reactions in guinea pig intestinal strips only after antigenic molecules had penetrated through the mucosa to the peritoneal surface. The relatively thick mucosal layer of the intestinal strips used in their experiments prevented rapid diffusion and penetration of antigen and they concluded therefore that ingested antigen must reach the intestinal muscle by way of the circulation to be effective in causing reactions in sensitized guinea pigs. Although it has been shown that unaltered food proteins such as egg can penetrate the intact gastrointestinal mucosa and enter the blood stream of human adults[10], the amount of unchanged protein absorbed normally is relatively small. Walzer[11] demon-

strated in man that the topical application of allergens to the surface of sensitized rectal or intestinal mucosa elicited less intense reactions than did contact by way of the blood stream with much greater dilutions of the same antigen. Walzer likewise noted the participation of the peritoneum in allergic inflammatory reactions.

Clinical experience indicates that relatively tremendous doses of antigen can be tolerated by sensitive humans when taken by mouth, as compared with

TABLE II

INCIDENCE OF MAJOR FOOD SENSITIVITIES IN 1,000 CONSECUTIVE PRIVATE PATIENTS

Male Age group	Wheat	Milk	Egg	Fish	Nuts	Other	Cotton Seed	Flax Seed	Total
Under 5	3	2	6	..	6	..	1	..	10
5 to 11	3	3	3	..	3	4	2	2	19
12 to 19	..	1	..	..	1	..	..	..	2
20 to 39	4	3	..	2	2	5	..	1	17
40 to 59	..	1	1	..	3	5	..	1	10
Over 59	1	..	..	..	1	..	..	..	3
Female Age group									
Under 5	1	4	2	1	4	2	1	..	9
5 to 11	..	1	..	..	2	2	1	..	5
12 to 19	1	4	..	1	2	..	..	..	8
20 to 39	1	5	3	1	1	5	..	..	22
40 to 59	4	3	2	..	1	1	1	..	10
Over 59	..	..	..	..	1	..	1	..	3
Total Male	11	10	10	2	16	14	3	4	61
Total Female	7	17	7	3	11	10	4	..	57
Combined Total	18	27	17	5	27	24	7	4	118

the extremely minute amounts of the same antigen which cause severe or dangerous shock when given parenterally so that rapid entry into the blood stream occurs. Spies and his associates[12] showed that the injection of as little as 100 micrograms of purified cottonseed antigen (CS-1A) induced reactions in passively sensitized skin sites, whereas 8,000 times this amount was required to cause a reaction when the same antigen was given by mouth. When crude cottonseed meal instead of the purified antigenic fraction was fed, the amount required was 20,000 times as great as that for the injected purified fraction. Patients who are sensitized to a given antigen, exhibit wide variations in the threshold of individual reactivity, and it is recognized furthermore that the permeability of the gastrointestinal mucosa for antigenic proteins may fluctuate. Inflammatory conditions such as acute gastroenteritis can increase permeability of the gastrointestinal

mucosa or organic lesions can impair its integrity so that unaltered antigenic protein can enter the blood stream more readily from the digestive tract. In infancy and early childhood the barrier of the gastrointestinal mucosa against penetration by undigested protein is less effective than in later years. For this reason symptoms of acute gastrointestinal allergy are more common during early childhood than in later life. Unequivocal gastrointestinal manifestations of sensitivities to foods present in early childhood frequently are lost in later life. Not infrequently one sees patients during early adult life who, for example, still have positive skin reactions to egg, but are able to eat egg without symptoms even though the history indicates that acute gastrointestinal or other allergic symptoms occurred after ingestion of even traces of egg during infancy. It is possible that such tolerance may be comparable to that developed by pollen sensitive patients after successful hyposensitization. However, the mechanism of the tolerance is not well understood. Excessive contact might again precipitate symptoms if the specific food were forced in the diet beyond the threshold of tolerance, especially during an illness associated with impaired integrity of the mucosal barrier in the gastrointestinal tract.

When chronic gastrointestinal symptoms occur, patients are prone to incriminate the last food eaten and to regard it as the cause of their distress. Such food suspicions often become cumulative and the list of avoided foods progressively longer and longer. Often, also, skin tests have been done by a technician and then, without consideration of inadequacies and limitations of such tests, these patients have been given food lists on which presumed sentitivities are indicated by plus marks as a guide to the degree of avoidance necessary. This documentary evidence of "sensitivity" to foods, most or all of which were previously eaten without the slightest distress, is used by the patient as the criterion for additional diet restrictions. Ultimately symptoms of malnutrition may be added to those of the pseudo-gastrointestinal allergy. Most of the symptoms of gastrointestinal allergy also occur in organic disorders. A patient who has clinical sensitivity to a food and who also has an organic disease of the gastrointestinal tract can be made symptomatically worse by continued contact with the specific food allergens to which he is sensitive. Patients who have peptic ulcer or ulcerative colitis and who, in addition, are clinically sensitive to milk almost certainly will be made worse if milk is continued or forced in the diet. This fact does not justify the conclusion that milk is an etiologic factor in the organic disease present. It cannot be overemphasized that actual sensitivity to a food must be demonstrated before exclusions, which would be undesirable otherwise, are made from the diet.

Andresen[13] believes recurring attacks of gastrointestinal allergy become continuous and are of major importance in the etiology of chronic ulcerative colitis. He found milk allergy, present in 80 per cent of his cases, the most common food offender. In our series of one thousand allergic patients we found only two who had chronic ulcerative colitis (Table III). In neither of these was allergy considered of etiologic significance nor were sensitivities to foods found. Nevertheless,

Andresen's observations extending over several years indicate the importance of a careful and unprejudiced search in such patients for evidences of gastrointestinal

TABLE III

SUMMARY OF SENSITIVITIES IN 28 PATIENTS WITH SYMPTOMS ATTRIBUTABLE TO GASTROINTESTINAL ALLERGY INCLUDING 7 IN WHOM GASTROINTESTINAL ALLERGY WAS FOUND

	Clinical Food Sensitivity	Asthma—atopic & inf.	Rhinitis—atopic & inf.	Rhinitis—non atopic	Dermatitis—atopic	Urticaria, etc.	Headache	Psychoneurosis	Pollen	Mold	Dust	Epidermals
1. M 5 G.I. allergy–abdominal pain	Orange	X	X						X	X		
2. M 6 G.I. allergy–abdominal pain	Egg	X	X		X				X	X	X	X
3. M 7 G.I. allergy–abdominal pain	Cocoa	X		X								
4. M 10 G.I. allergy–abdominal pain	Celery								X			
5. M 9 Pyloric stenosis–history	Milk	X	X								X	
6. M 21 G.I. allergy–indigestion	Cocoa		X				X	X	X		X	X
7. M 33 Colitis–spastic	Mustard	X	X		X				X		X	X
8. M 5 Celiac disease				X								
9. M 29 Peptic ulcer–gastroenterostomy		X	X						X		X	X
10. M 57 Peptic ulcer	Mustard-Flaxseed	X	X			X			X		X	X
			X						X		X	X
11. M 44 Peptic ulcer–perforated–history												
12. M 61 Peptic ulcer–chronic ulcerative colitis (inactive)		X		X								
13. M 43 Chronic ulcerative colitis			X								X	
14. M 48 Duodenal ulcer		X	X					X			X	X
15. M 41 G.I. neurosis–indigestion			X						X			
16. M 41 G.I. neurosis–anxiety			X					X			X	
17. M 46 G.I. neurosis–psychaesthenia								X				
18. M 63 G.I. neurosis–indigestion		X										
19. F 29 Gastric resection (?) history			X				X		X			
20. F 37 G.I. neurosis–indigestion												
21. F 21 G.I. neurosis–diarrhea			X					X			X	
22. F 29 G.I. neurosis–hysteria				X				X				
23. F 24 G.I. neurosis–hysteria		X	X				X	X	X		X	
24. F 26 G.I. neurosis–anxiety				X				X				
25. F 33 G.I. neurosis–diarrhea												
26. F 45 G.I. neurosis–indigestion							X					
27. F 60 G.I. neurosis–diarrhea												
28. F 65 G.I. neurosis–diarrhea								X				

allergy. It again must be emphasized that the low incidence of gastrointestinal allergy found in our series of allergic patients must not be interpreted as evidence that allergy may not be a potent cause of acute digestive symptoms. Our survey

indicates only that in a fairly large group of allergic individuals chronic gastrointestinal allergy was not a frequent cause of symptoms.

The diagnosis of gastrointestinal allergy is difficult. There are no laboratory procedures or diagnostic routines that can be substituted for sound clinical judgment. Roentgen studies[14] have shown changes in gastrointestinal allergy conforming to a general pattern of disturbed motility. Usually there is hypermotility evidenced by rapid transit of the barium to the cecum. At times there is delayed gastric emptying, hypertonicity or less often hypotonicity of the small bowel, and segmentation of the barium column. In many patients, however, motility changes occurred before the test allergen was fed, and none of the changes observed in roentgen studies could be attributed exclusively to allergic reactions. It is apparent therefore that roentgen studies are of negligible importance both in the diagnosis of gastrointestinal allergy and in the identification of specific allergens when that condition is known to be present.

Rigid elimination diets often are continued indefinitely without medical advice and can lead to semistarvation. Depletion of protein reserves including antibody globulin with resulting lowered resistance to infection may occur from such ill-advised diets. In our own practice, as previously mentioned, a modified provocative diet is used to identify or exclude major food offenders, Later forced trial feeding and withdrawal of suspected food aids in recognition and identification of those foods clinically responsible for symptoms. These latter trials are guided by the history, especially of food idiosyncrasies in childhood, and by other clues provided by the allergy study and diet diary. I believe this approach to be the most satisfactory method for the recognition of clinically important food sensitivities. A symptom-free period during trial elimination of a suspected food is suggestive, but is not sufficient evidence alone to justify the diagnosis of hypersensitivity. In addition symptoms must be reproducible at will when the suspected food is included in the diet. Even this evidence will not exclude possible psychogenic causes unless the trial food has been given in an unrecognizable form. We have found with surprising frequency that patients who believed that they had symptoms from one or more major foods were convinced that no intolerance was present after a provocative diet had been eaten for a week without signs of distress. On the other hand, when aggravation of symptoms does occur on such a diet, further well planned diet trials guided by all other available information can lead to the identification of foods responsible for symptoms in the relatively small group of patients who do have true gastrointestinal allergy.

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Discussion

Dr. I. Snapper:—It is certain that in the gastrointestinal tract allergy exists. We have all seen recurring allergic signs in the gastrointestinal tract after ingestion of certain foods. It is regrettable that allergists have not been too critical in their approach to this problem. The way in which Dr. Squier has presented this difficult question, basing his opinion mainly upon the results of exclusion diets and provocative diets, is certainly the correct approach. Even if the skin reactions cannot be trusted for the diagnosis of gastrointestinal allergy, there are, as Dr. Squier has demonstrated, other methods which reveal the clinical importance of gastrointestinal allergy.

Dr. Walter Freymann (*West New York, N. J.*):—Have you ever encountered allergic conditions in the form of migraine? I personally suffer from an allergy to venison, which discovery I made when I was 14 years old. I shot hares myself on a farm and after eating them experienced violent headaches, scotoma with vomiting, that means an attack of severe migraine. These attacks come on about 4 to 12 hours after ingestion of hare meat. After having had this type of migraine attack about 12 to 14 times I consulted our family doctor, who in turn called in two other physicians in consultation. All three doctors agreed that I did imagine the connection between eating of hares and my violent migraine attacks. Up to this day I get a migraine attack, followed by vomiting, whenever I eat venison of any kind.

Dr. Theodore L. Squier:—I am very sorry, Dr. Freymann, that I can contribute very little on that subject. I always look in proven cases of migraine for

allergic reactions to foods. I have not found reactions to foods as a cause of migraine. They may exist. There are causes for migraine that we do not understand. One must remember that an antigen antibody reaction is an essential before any reaction can be attributed to allergy.

I wish to thank Dr. Snapper for his discussion.

DIFFERENTIAL DIAGNOSIS OF THE MULTIPLE SYNDROMES OF THE UPPER GASTROINTESTINAL TRACT*

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The human body is a powerful chemical plant, closely compact in a miniature housing which averages 150 pounds in weight. The gastrointestinal tract is the central thoroughfare, the main supply line for the entire body. Partly because of the anatomical compactness of the body there is a great overlapping in spheres of physiological and chemical activity. One of the areas of greatest heterogenicity of activity is the area which for purposes of discussion will be referred to as the digestive axis. Most physicians at one time or another have been perplexed by the remarkable overlapping of symptom complexes associated with the various diseases of the digestive system and particularly those of the upper gastrointestinal tract. In the analysis of these diseases the clinician has considerable advantage if he is ever mindful of certain basic facts which help to explain the rationale of the complex and often perplexing picture of dyspepsia. One should visualize these problems in the broad panorama of anatomical structure, physiologic activity and pathological change.

Let us first consider the embryological development of the organs in the digestive axis. It will be recalled that the gallbladder, the liver, the pancreas, the stomach and duodenum with all their connecting ducts developed from the primitive foregut. During the period of rotation, the duodenal folds may fail to unite snugly around the entrance of the pancreatic and common bile ducts at the papilla of Vater and the ground work is laid for the development of duodenal diverticula in the adult. This will be referred to later in the discussion. We may liken the focal axial point in the digestive sphere to the hub of a wheel.

In the adult organism the anatomical connections of the intra-uterine development are maintained. The cystic duct of the gallbladder joins the hepatic duct to form the common bile duct. At the point where the common bile duct reaches the duodenum it joins the duct of Wirsung of the pancreas and enters the duodenum through the papilla of Vater. This point of exit is guarded and controlled by the common constrictor muscle, the sphincter of Oddi. There is wide and extensive anastomosis of the arterial venous and lymphatic vessels of the organs within the sphere of the digestive axis. Sympathetic nerve impulses are supplied to these organs by common branches of the celiac plexus, counterbalanced in healthful states, by parasympathetic action from the gastric and hepatic branches ot the vagus.

Physiologically, the evidence is still more convincing of the remarkable interdependence of the organs about the digestive axis. So that it is not only

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the anatomic overlapping of structures in the upper gastrointestinal tract but an overlapping of physiologic activity which explains the heterogenicity of symptoms in this area.

The interdependence and overlapping of digestive functions are illustrated in many ways. The ptyalin action upon cooked starches and peptic action upon complex proteins in the stomach may be taken over entirely by pancreatic digestion for example in achylia gastrica of pernicious anemia or after gastrectomy, and life goes on more or less normally. In severe pancreatic disease producing pancreatic achylia or after pancreatectomy digestion may be carried out by the enzymes of the gastric juice and the succus entericus. During attacks of hepatitis and after cholecystectomy, biliary functions are compensated by physiological adaptations in the upper gastrointestinal tract.

When disease strikes in either the biliary system, the stomach, the duodenum or the pancreas the compensatory physiological activity is such that the disorder may be considerably advanced before noticeable symptoms develop. Thus, the overlapping of digestive function in health has its counterpart, the overlapping of dysfunction in disease. The so-called ulcer syndrome may be simulated by biliary dyskinesia, duodenitis or hypertrophic gastritis. The so-called gallbladder symptom complex may be simulated by chronic atrophic gastritis, chronic relapsing pancreatitis, choledochitis and gastrointestinal malignancy.

Pathologic Change

To illustrate some of the more commonly confused clinical entities referable to the upper gastrointestinal tract, representative cases will be discussed. I should like to dismiss at once some of the comonly seen disorders of the upper gastrointestinal tract as offering no diagnostic problems. And, as a matter of fact, with reference to far advanced malignancy, cholecystic disease and typical ulcer, these may be eliminated from discussion. On the other hand these disorders in their incipiency may manifest *very similar symptons.* For this discussion some of the less commonly diagnosed conditions will receive the greater emphasis.

Case 1:—A female graduate sociology student, age 32 years, received treatment off and on for two years in a clinic where psychosomatic enthusiasm ran at a rather high level. She was treated for "nervous indigestion." The concretion pictured in the chronically inflammed gallbladder mucosa represents chronic low grade cholecystitis with so-called silent stones.

Twenty years ago chronic cholecystitis without stones was the most commonly diagnosed disorder of the upper abdomen. It had gone out ahead of chronic gastritis nearly a decade before. Empirical gastritis of the pre-World War I days had fallen into disrepute when the pathologists failed to confirm its widespread distribution at the postmortem table. Today, after a decade and a half of observa-

tions with the flexible gastroscope, chronic gastritis is again statistically in the lead. However, it is regarded as having perhaps less clinical significance than it appeared to have during the first two decades of the century. Very often, but not always, there are other more significant digestive disorders co-existing with chronic gastritis. These changing clinical concepts from decade to decade bespeak the diagnostic importance of the problem of "overlapping" symptons in disorders of the upper gastrointestinal tract.

Calculous Cholecystitis and Gastric Malignancy

Cholecystitis is occasionally complicated by other gastrointestinal diseases.

Case 2:—A middle-aged pullman porter complained of vague abdominal distress. Cholecystography showed a large gallbladder with poor concentration. X-ray of the stomach and gastroscopy were negative. Surgery was considered but deferred, because of the patient's nutritional state and because the symptoms were those due to the associated cholecystitis usually not relived by surgery. Under medical management the patient gained 16 pounds in three months with complete relief of symptoms. Symptoms recurred with beginning weight loss during the sixth month. Re-examination revealed carcinomatous ulcer. Patient is living and well six years after cholecystectomy and partial gastrectomy. In this case carcinoma probably developed while the patient was under care for cholecystitis.

Duodenal Ulcer and Cholecystitis

In several instances we have observed active duodenal ulcer and cholecystitis in the same individual. The overlapping of symptoms in such a case may confuse the clinical picture. The diagnostic study of the stomach should always be accompanied by studies of the gallbladder and often the remainder of the G-I tract as well.

Case 3:—In the case of W. C., male, age 35, cholecystectomy was performed after treatment of the duodenal ulcer. The scar was seen at surgery.

Postcholecystectomy Syndrome

Case 4:—A female patient aged thirty-five had a cholecystectomy because of gallstones. Two months later there was recurrence of right upper quadrant pain and intermittent jaundice followed by attacks of vomiting. The clinical picture strongly suggested one of the elements of the so-called postcholecystectomy syndrome probably residual stone in the common duct. The patient was re-explored and a common duct stone removed. Cholangiography at the operating table indicated no further obstruction in the biliary ducts and the choledochogram shows an unobstructed common duct.

During the last few years there is a steadily increasing awareness among gastroenterologists of the frequency with which *subacute to chronic* pancreatitis

may explain the symptoms of the chronic dyspeptic. This clinical picture in the past has usually been confused or mistaken for cholecystitis, gastritis, nervous stomach, etc.

Chronic Relapsing Pancreatitis

Case 5:—A male ambulatory patient W. E., aged 30, presented himself with symptoms of epigastric distress and bloating. He became worse after meals and sometimes painful enough to lie down or double up. On such occasions the pain radiated across the left upper quadrant and to the back. There had been several periodic attacks since the days in the army 3 years before. X-rays of the stomach and gallbladder were negative. Gastric acidity, urine and stool were normal. Low residue diet and symptomatic treatment gave only transient relief. A few weeks later the patient was rushed to the hospital with severe upper abdominal pain and expired with the shock picture of a catastrophic abdomen. At autopsy the findings were *acute hemorrhagic pancreatitis with abdominal pancreatic necrosis*. The clinical episodes were due to chronic recurrent or relapsing pancreatitis.

Acute Cholecystitis and Acute Edematous Pancreatitis

Case 6:—A bedfast female patient, aged 35, was seen in the home writhing in pain. Following hospitalization the temperature rose to 104°, marked tenderness and pain in the *right upper quadrant* with radiation across the left upper abdomen. X-ray showed questionable visualization of the gallbladder and negative stomach. Serum amylase was within normal limits (80 units), stools were normal, urine was negative for sugar but glucose tolerance test showed a diabetic type of curve with spilling of sugar in the urine. Diagnosis: *Acute cholecystitis* with *acute edematous pancreatitis*. Patient made an uneventful recovery.

Chronic Recurrent Cholecystitis. Acute Edematous Pancreatitis Superimposed Upon Chronic Recurrent Pancreatitis

Case 7:—A 50-year old male ambulatory patient complained of left upper quadrant pain more or less constant and unaffected by eating. There was some loss of weight and constipation. X-rays showed the stomach pushed up to the left and anteriorly. Cholecystogram showed a nonfunctioning gallbladder. Serum amylase was moderately high—175 units. The glucose tolerance curve was normal. Surgical exploration revealed an enlarged, edematous pancreas through which could be felt an underlying hard organ. There was a low grade peritonitis without necrosis. The gallbladder and common duct were greatly enlarged, thickened and dilated. No stones were detected. Diagnosis: *Chronic recurrent cholecystitis. Acute edematous pancreatitis superimposed upon chronic relapsing pancreatitis.*

Carcinoma of the head of the pancreas, before jaundice or carcinoma of the body develops, may simulate many of the disorders already discussed. The next slide shows carcinoma of the body of the pancreas. The roentgenogram shows gastric compression and displacement to the left by the tumor. A microscopic section of the pancreas shows undifferentiated carcinoma. When carcinoma invades the head of the pancreas with obstruction to the common duct, the progressive jaundice which follows and other changes detectable by liver function studies make this diagnosis ofttimes less difficult.

When carcinoma has its origin in the ampulla of Vater it may be very difficult and at times impossible to distinguish it clinically from carcinoma primarily involving the head. When such a differential diagnosis can be made the surgical approach may be simplified in the case of ampullary carcinoma greatly improving the prognosis. This slide shows ampullary carcinoma with common duct obstruction. Marked dilatation of the common duct and pancreatic duct may be seen in the gross specimen. The microscopic section shows the tumor invading duodenal mucosa. The x-ray shows a normal duodenal loop.

Diverticula are particularly prone to occur in the second portion of the duodenum at or near the papilla of Vater, congenital weakness of the wall in this area predisposes to this condition. These defects are referred to by the French as "diverticules peri-vateriens". Diverticula in this area as elsewhere may become inflamed. Duodenal diverticulitis may produce symptoms very similar to duodenal ulcer. In this case diverticula occurred not only in the duodenum but also in the esophagus.

Duodenitis, peri-duodenitis, duodenal parasites should certainly be mentioned. Time will not permit discussion.

Peptic ulcer may be closely simulated by chronic hypertrophic gastritis. The distress is often described as gnawing or burning. It comes on usually one to two hours after meals and may be relieved by food or alkaline powders. These cases may be confusing when x-ray studies reveal a negative stomach. All cases presenting the rhythmic distress of ulcer in which an ulcer lesion is not found by x-ray studies should be studied gastroscopically. The mucosa presents multiple nodules on the crests of folds and in the crevices between folds. The nodules are flat-topped with polygonal bases and arranged so as to form the so-called cobblestone pattern in many instances. The mucosa is usually pale pinkish gray and velvety with diminished highlights. Often there are also scattered tiny superficial erosions with gray bases. It may be that the ulcer-like symptoms are produced by these tiny erosions. Atrophic gastritis, uncomplicated, may simulate cholecystitis, etc.

Hypertrophic gastritis is very often associated with duodenal ulcer. In the case of a young man, 30 years of age, there was extensive hypertrophic gastritis associated with ulcer of the duodenum. The x-ray shows the deformity of the

bulb but does not reveal the gastritic changes. The latter is diagnosed by gastroscopy. His symptoms were severe and resistant to treatment. These cases usually require bed rest and rigid management.

The literature shows an increasing number of cases of duodenal ulcer with hypertrophic gastritis associated with antral spasm or persistent antral deformity or so-called tumor simulating gastritis.

The illustrations which follow will point up the importance of examination of all the organs of digestion in every case of persistent dyspepsia by multiple diagnostic methods.

A 45-year old woman presented symptoms of the so-called typical ulcer syndrome. The fractional gastric analysis showed a hyperacidity curve after histamine stimulation. Antral deformity and probable ulcer niche were seen roentgenologically. The diagnostic impression was benign ulcer with antral spasm. Gastroscopically, extensive hypertrophic gastritis with antral narrowing was seen. The patient was therefore treated intensively on an ulcer type of management. Three months later the x-ray showed little or no change in the antral deformity, but there had been marked clinical improvement, including gain in weight. During the next 2 months her symptoms tended to recur when medication was temporarily removed. There was still no definite improvement in the antral narrowing. Resection was insisted upon. The gross specimen showed extensive nodulation on the crests of folds and the cobble-stone pattern between the folds. Near the pylorus there was an extensive partly-healed ulceration. A short distance away there appeared a large node. Microscopic section through the ulcer, itself, showed adenocarcinoma. This microscopic section was taken through a nodule of hypertrophic gastritis. Directly beneath the nodule in the submucosa infiltrating carcinoma cells can be seen. The nodule near the ulcer was metastatic carcinoma. The final diagnosis was hypertrophic gastritis with a carcinomatous ulcer simulating benign peptic ulcer. This case is of particular interest because it is much more common to see atrophic rather than hypertrophic gastritis associated with gastric cancer.

Case of E. R., age 55 years, who presented himself with epigastric pain partly relieved by food and powders. Nausea and vomiting had recently intervened. Episodes of varying degrees of severity had occurred for the last few years. There was a normal gastric acidity curve. Stools were negative for occult blood. The roentgenogram showed an irregular antral deformity diagnosed as carcinoma. The deformity is illustrated in this slide. The second film taken months later showed only a slight decrease in the extent of the deformity. Gastroscopy showed two ulcer craters on the lesser curvature. The base of one was covered with a homogenous white adherent mucus. The other was covered with a black, adherent exudate charactristic of old blood. Both were characteristically benign, with sharply punched out regular appearance. The surrouding mucosa was a normal homogenous orange-red color even in the narrowed antral region. Repeated gastroscopy

offered further evidence of benignancy. The clinical symptoms seemed to justify a period of medical management. Improvement was so striking that when surgery seemed indicated the patient would not consent. Surgery seemed indicated as a precautionary measure against cancer when a large portion of the deformity persisted. One year later, during an acute upsetment, following a dietary indiscretion, the patient was hospitalized and converted to surgery. The gross specimen showed the ulcer with typical radiating folds which still appear to be benign.

Microscopic section further confirmed the benign character of the ulcer and the surrounding mucosa. Eight years later the patient is living and well and still working at his occupation as a mail carrier. The final diagnosis was benign gastric ulcer with persistent antral deformity simulating gastric carcinoma.

A 40-year old male complained of symptoms suggesting an ulcer syndrome. The roentgenologist reported an ulcer crater fluoroscopically. However, a careful inspection of the film shows a fairly good meniscus sign, suggesting carcinoma. Gastroscopically the ulcer was diagnosed carcinoma. The gross specimen presents a picture very similar to that seen at gastroscopy. An ulcer "en platau", ulcer on a hill (comment). Microscopically, the cancer was confirmed.

This review of cases *illustrating* overlapping symptoms referable to the upper abdomen by no means describe all the digestive disorders which may simulate each other. In the every day differential diagnostic study of this group one must often consider disorders of the colon and very often disorders of the genitourinary tract, coronary insufficiency and other cardiac lesions. Any of these may be the *primary cause* of epigastric distress. To this group we must add many remote diseases which may reflexly evoke dyspeptic symptoms in the upper abdomen. Among them are the very important group of allergies. Lastly, there is that group of ever increasing popularity, the primary *neuroses* or the *psychosomatic disturbances* of digestion. The latter group of disorders is usually diagnosed by the process of elimination and should not be entertained as the sole cause of upper abdominal symptoms until all *organic possibilities* have been eliminated.

I hope that this review will serve not to *over-emphasize* the perplexity of the problem. On the contrary, I have tried to point out that the modern *technics of applied physiology, biochemistry, precision roentgenology and gastroscopy* when combined with adequate clinical experience, the hodge-podge of upper abdominal dyspepsia is capable of analysis into *distinct clinical entities*.

Discussion

Dr. I. Snapper:—It is interesting that Dr. Berry finds lots of gastritis in cases of ulcer of the duodenum. As Dr. Berry has already intimated, the history of interest in gastritis has had many ups and downs. When Kussmaul first introduced the stomach tube, he diagnosed gastritis whenever lavage of the stomach produced

much mucus and from then until 1910 everybody diagnosed gastritis by gastric lavage. Then it appeared that the pathologist did not find gastritis in the stomach in autopsies performed one or two days after death and no respectable clinician diagnosed gastritis any more until the gastroscopists made gastritis popular again. Even in this country many clinicians now agree that gastritis may be a cause of ulcer. In this connection, it may be pointed out that gastritis may well play a role in the causation of the gastrojejunal ulcers which were so frequent after gastroenterostomy and which are still occasionally seen after subtotal resection. These gastrojejunal ulcers were considered to be due to the fact that acid reaches the jejunum. However, the gastroscopists always find a severe gastritis after gastroenterostomy. Since gastritis of the antrum so often accompanies ulcer of the duodenum, we may perhaps speculate whether the gastritis of gastroenterostomy is not one of the major causes of gastrojejunal ulcer.

Patients with arteriomesenteric closure after stomach operations may for one or two weeks vomit all food mixed with large amounts of bile. This ultimately leads to tetany and sometimes even to death. Such cases are nowadays rare. This condition does not only occur after gastroenterostomy but also after shock. Occasionally one sees a patient with a fracture of the neck of the femur, who after having been in shock for a short time after the accident, vomits for many days. In these patients, there are often signs of pyloric obstruction. Such patients have an arteriomesenteric closure which is, however, a little different from the cases Dr. Berry described. After a traumatic shock or after anesthesia, the arteriomesenteric closure is caused by the marked dilation of the stomach. The latter hangs over the ligament of Treitz, which is the reason why the pylorus is obstructed.

This picture of arteriomesenteric closure has been somewhat forgotten. When these patients, after anesthesia or trauma, vomit for several days, too often hazardous diagnoses of acute carcinoma or acute ulcer are made and operations are planned. When such a patient is told to lie on his abdomen and when strychnine injections are given, the arteriomesenteric closure disappears rapidly and the vomiting stops.

HEMANGIOMA OF THE SMALL INTESTINE

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Hemangioma of the small intestine is a rare tumor. Hansen[1] found 66 cases recorded in the medical literature between 1860 and 1948 and added three of his own. Stratton[2] has reported another instance. Its rarity seems to justify the report of two more cases.

Kaiser and Obendorff classified these tumors into four groups: (1) multiple phlebectasia; (2) cavernous hemangioma, diffuse or circumscribed; (3) simple capillary hemangioma; (4) angiomatosis localized to the gastrointestinal tract. Hansen divided them on the basis of the histology into three groups: (1) simple hemangioma consisting of capillaries, dilated or nondilated, and separated by

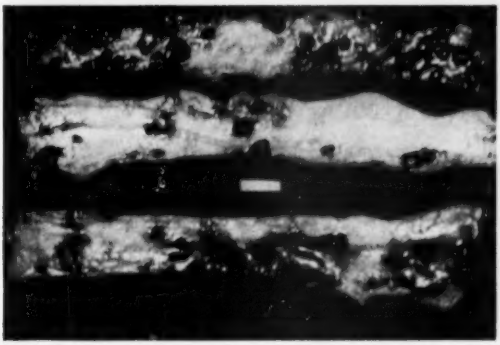

Fig. 1—Case 1. Multiple hemangioma of the small intestine.

little or abundant fibrous strands; (2) cavernous hemangioma, consisting of large blood-filled communicating spaces lined by endothelium and having little or no stroma; (3) combined hemangioma presenting combinations of the above types. Any one of these types may be solitary or multiple.

Case Reports

Case 1:—The patient was a negress, 39 years of age who, three days prior to admission to the hospital, became ill during an alcoholic bout with nausea followed by vomiting and diffuse mild nonradiating abdominal pain. During the previous year, three similar episodes had occurred, the last one three months

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before the current attack. There was no history of food intolerance, hematemesis, diarrhea, melena or anorexia.

On physicial examination, the only positive findings were mild diffuse abdominal spasms without rebound tenderness, a tachycardia of 120 and the presence of a pelvic mass considered to be ovarian. The blood pressure was systolic 110, diastolic 56. Anemia was absent: Hgb 16 gm. HBC 4,750,000, hematocrit 46 mm. There was a moderate leucocytosis of 14,500 with a polynycleosis of 75 per cent. The urine contained sugar 1 plus and a few red and white blood cells. The blood sugar level was 171 mg. per cent and the serum amylase 42 mg. per cent.

Nine hours after admission, the patient suddenly lapsed into deep shock, the blood pressure was unobtainable and the pulse rate rose to 156. She failed to respond to four units of plasma. The temperature rose to 103, she became anuric and died in coma ten and a half hours later.

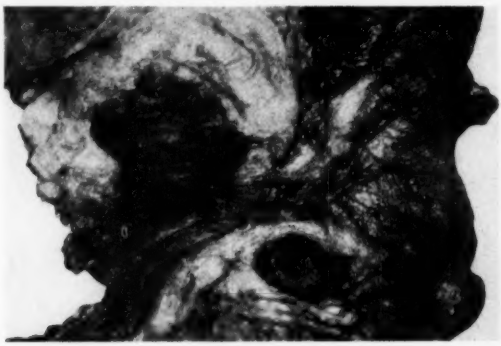

Fig. 2–Case 2. Single hemangioma of the duodenum.

Autopsy (8459) was performed 38 hours after death. Only the pertinent findings are given. The small intestines, for a distance of 175 cm. reaching within 115 cm. of the ileocecal valve, were studded with innumerable small firm dark red to black sessile polypoid masses (Fig. 1) and contained a small amount of fresh blood. The point of hemorrhage could not be ascertained. Histologically the masses proved to be groups of extraordinarily dilated submucosal capillaries. The only other finding of note was the complete destruction of both adrenals by chronic caseous tuberculosis and the presence of rather small chronic active lesions in the lungs.

Comment:–This patient presented two features of note, the extensive capillary hemangiomas of the small intestines and the evidence of Addison's disease. Addison's disease in the negro is a relatively rare condition, only 22 cases being reported up to 1943[3]. The small amount of intestinal hemorrhage seemed insufficient to explain death in shock. It is theoretically possible, however, that with

the extensive destruction of the adrenals, a relatively minor blood loss may have been sufficient to produce the profound shock exhibited by the patient.

Case 2:—The patient was a negro 83 years of age who had been under observation because of prostatic obstruction and who died of acute myocardial infarction associated with calcific aortic stenosis. There were no symptoms referable to the intestinal tumor.

At autopsy (8510) there was found in the second portion of the duodenum, 5 cm. distal to the papilla, a small soft dark blue-black sessile polyp measuring 2 x 2 x 4 cm. Histologically it proved to be a submucus cavernous hemangioma.

Comment:—The hemangioma was an incidental finding at necropsy in an individual dying of an unassociated condition. As far as could be determined, it had been completely silent and had never been associated with any evidence of rupture or intestinal bleeding.

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NONSPECIFIC GRANULOMA OF THE ILEUM IN A LUETIC WITH FOREIGN BODY OBSTRUCTION

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The etiology of nonspecific granuloma of the intestine has been a subject of speculation from the time Tietze[1] in his comprehensive monograph in 1920 first called attention to this category of tumors. Attempts were made to clarify the origin of these granulomata according to either intraluminal or extraluminal causes. The former were considered to have set off the original inflammation by an injury to the mucosal surface of the bowel. In this category are foreign bodies within the lumen, small ulcerations, diverticulitis or appendicitis[6,7]. Among the extraluminal irritants which seem to have affected the bowel wall by contiguity are foreign bodies in the abdominal cavity, (pursestring sutures, lap sponges, splinters) which have been found to be the focal points, around which the chronic productive inflammatory process seems to originate. There has been a divergence of views regarding the pathognomonic aspects of this condition (Mock[2], Dudley and Miscall[3]). While Wilensky[4] in 1932 felt that nonspecific granuloma offered no characteristic clinical concept, beause it was too protean and indefinable in its etiology and symptoms, Crohn, Ginzburg and Oppenheimer[5] in the same year introduced the term regional ileitis, which temporarily set aside one group of these granulomata as a new clinical entity.

Various authors have postulated the possibility of an impairment of the local mucosal circulation preceding a low grade infection and a resulting inflammatory reaction. The latter is characterized by necrosis and reparative processes acting and reacting with a gradual development of an inflammatory mass. If the reparative process predominates early, one finds a constricting or stenosing granuloma. Systemic infections such as tuberculosis and lues have been cited as possible predisposing factors, which by lowering local tissue resistance may lead to mucosal changes, which favor invasion by organisms capable of setting up a granulomatous reaction. There is, however, no substantiation in the literature of an actual coexistence of the two conditions or their casual relationships. This situation would of course not be identical with gummata of the intestinal tract, which, even though they have been reported, are exceedingly rare, outside of the stomach and the rectum.

The following case poses the problem of etiology of a granulomatous mass in a luetic patient, who ingested an obstructing foreign body (plum pit) while under diagnostic investigation for the palpable abdominal tumor.

From the Department of Gastroenterology of the Jewish Hospital of Brooklyn.

Case Report

A. O., a 49 year old Jewish housewife was admitted to the Surgical Service of the author (D.F.) on 8/12/49, complaining of intermittent right lower abdominal pains without associated gastrointestinal symptoms. There was no melena or frank blood in the stool. The pains had been present for several weeks and were cramplike in nature, disappearing at times for several days. She had been examined several weeks prior to her hospital admission and was found to have a firm, mobile nontender mass in the right lower abdomen of small grapefruit-size, which seemed to rise out of the pelvis. It was considered to be a possible peduncu-

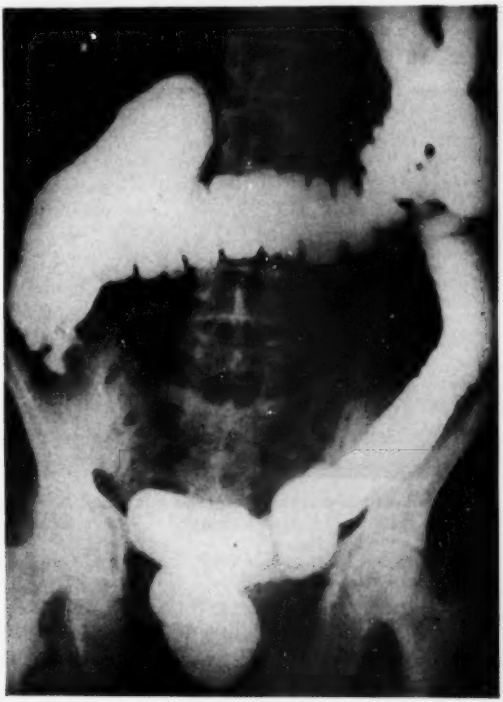

Fig. 1—Filling defect in ascending colon, due to extrinsic pressure.

lated fibroid uteri, and the patient was advised to have it removed. She delayed the operation because she was relatively comfortable. Several days prior to admission the patient swallowed a plum pit. She was immediately aware of the fact, but did not tell about it. Subsequent to that incident, however, her pains became more constant and severe and she consented to surgical intervention.

A review of her previous hospital record revealed that the patient was a known luetic, having received antiluetic treatment with her three pregnancies, the last in 1937. The placenta at that time showed typical luetic changes. She ap-

parently received no further treatment, thereafter, and her Wassermann and V.D.R.L. reactions remained positive up to the present.

The physical examination on admission revealed a fairly well nourished woman with a good hemic component, who was in no acute distress. She had a nodular enlargement of the thyroid. Her skin was clear, no adenopathies were present. Heart and lungs presented no abnormalities. B.P. 142/70. Her abdomen revealed the mobile mass in the right lower quadrant, as described above, which was slightly tender to palpation. Pelvic and rectal examinations appeared normal. There were no unusual neurological findings.

Laboratory data:—Blood ct: Hgb 13 gm. 9,600 WBC, normal differential count—Total proteins 6.5 gm. A/G ratio, I. Blood chlorides 330 mg. per cent.

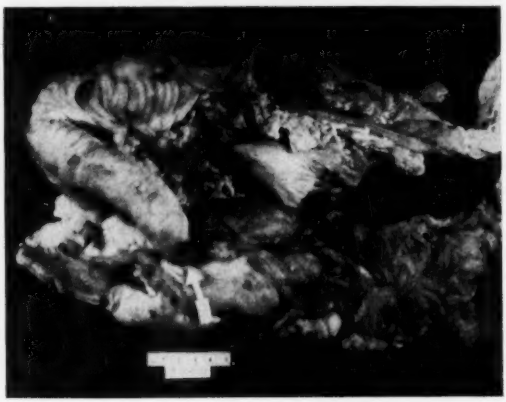

Fig. 2—Plum seed embedded within constricting granuloma near the ileocecal valve causing partial obstruction.

Sugar, 95 mg. per cent. Urea 14.2 mg. per cent. Urine: Alb. neg, Sugar, neg. Microsc., occ. WBC.

A barium enema done prior to admission revealed a filling defect of the ascending colon and an upward displacement considered due to extrinsic pressure (Fig. 1). A study from above was not undertaken because of the risk involved. The preoperative diagnosis was 1) Paraovarian cyst or interligamentous fibroid. 2) Possible malignancy of the ascending colon or terminal ileum.

At operation, a firm mass of the ileocecal junction was found. The terminal ileum and its mesentery were adherent to the cecum in this region; the terminal ileum was distended and thickened. Macroscopically, it was most difficult to distinguish between an inflammatory and neoplastic mass of the cecum. Therefore, radical excision was decided upon. A right hemicolectomy and resection of the terminal ileum and an ileotransverse colostomy were performed. The clinical diagnosis was that of a carcinoma of the cecum.

The pathological report described a specimen consisting of 40 cm. of terminal ileum, leading into a firm fixed mass approximately 15 cm. in length. The mesenteric lymph nodes in this area were enlarged, measuring up to 2 cm. in diameter. The mucosa of the ileum was congested, and approaching the cecum, it became thickened up to .6 cm. About 40 cm. from the proximal end of the specimen, there was a constriction of the lumen which contained a plum seed 1 cm. in diameter, causing obstruction (Fig. 2).

Microscopically, the mucosal surface showed, in places, poor staining and infiltration with mononuclear and some polymorphonuclear cells. In the deeper portions, lymphfollicles were seen and a denser infiltration with mononuclear cells, plasma cells and some polymorphonuclear leucocytes were present. The same findings were present in the intermuscular connective tissue and the serosa.

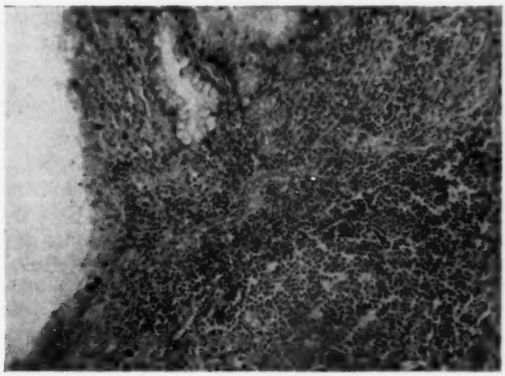

Fig. 3—Typical granulomatous changes with infiltration by mononuclear cells, plasma cells and some polymorphonuclear leucocytes. Absence of giant cells.

No giant cells were seen (Fig. 3). The lymph nodes were the seat of an inflammatory reaction. The pathological diagnosis was that of a constricting ileitis and obstruction of the lumen by a plum pit.

Comment:—This case again illustrates the diagnostic difficulties encountered in the vast majority of granulomata of the intestines, which, prior to operation, are considered to be malignant tumors. The gross specimen, even after resection, had the appearance of a carcinoma of the colon, until the pathologist supplied the true answer, after microscopy. The obstructing foreign body, which in several other cases, was looked upon as the convenient causative factor, was ingested while the patient was under investigation for the abdominal mass, and it thus could have played no part in the etiology. The absence of giant cells, histologically, also substantiates this fact. The role of the patient's luetic condition as a predisposing factor is, of course, conjectural. There were no perivascular infiltrations present on a close review of the slides.

The treatment of granuloma of the intestinal tract is surgical. Occasionally, the mass may diminish in size as a result of a side-tracking anastomosis. This procedure is, however, not curative but palliative and leaves the possibility of an intermittent reactivation of the pathological process, which may act as a focus of constant irritation and infection.

Added to this danger, is the fact, that it is very difficult to differentiate, at times, between malignancy and benign chronic inflammatory reaction. Thus, if less than a radical excision is done, the patient is exposed to an inadequate procedure and robbed of the chance for an early and radical cure.

Summary

A case of constricting, nonspecific granuloma of the ileum in a luetic woman with an obstructing plum pit is presented. The foreign body was ingested at a time when the patient's abdominal mass was known to exist.

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ATTEMPTS TO PREVENT PANCREATIC FAT NECROSIS*

1. Experiments With Soybean Antitrypsin

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In previous papers[1,2] a simple method for producing extensive pancreatic fat necrosis in the dog was described. The method consists in leaving the main pancreatic duct freely exposed in the abdomen after it has been excised from the duodenum with a circular flap of duodenal wall, approximately 2 cm. in diameter, attached to it. Of 20 dogs submitted to this procedure 16 (80 per cent) died with extensive intraperitoneal and intrathoracic fat necrosis between the 2nd and the 8th postoperative day, the majority of them on the 3rd or 4th postoperative day. There is no other procedure which yields fat necrosis in a similarly high percentage of experiments and with equally uniform results. This method seemed, therefore, to lend itself to the critical study of attempts at preventing pancreatic fat necrosis or modifying its course.

While pancreatic fat necrosis is principally due to the action of pancreatic lipase on fat tissue, presence of pancreatic trypsin is thought to be essential to initiate this digestive action. Hence the formation of fat necrosis might be prevented by inhibiting the action of trypsin. Kunitz[3] has shown that a substance isolated from soybean, soybean antitrypsin, produces an inactive compound with trypsin. We decided to try the prophylactic value of this substance† in the above-described procedure.

Method

Nineteen male and female mongrel dogs, weighing between 4 and 13 kg. were subjected to the operation described above, and 1 gm. of antitrypsin suspended in 50 ml. of normal saline was instilled into the peritoneal cavity before the abdomen was closed. In 2 dogs, additional intraperitoneal injections of 1 gm. of antitrypsin in saline were administered daily for 3 days after the operation. As in the previous experiments, the dogs were not fed pre- and postoperatively,

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†Soybean antitrypsin was kindly supplied by Dr. E. A. Sharp and Mr. E. C. Loomis, of Parke-Davis and Co., Detroit, Mich., and by Mr. F. H. Hafner, of General Mills, Minneapolis, Minn.

but water was given freely after the operation. Penicillin and streptomycin were administered for 3 days following the operation.

Results

Ten of these 19 dogs died with extensive fat necrosis, similar to that described in our previous work[1,2]. The 2 dogs with repeated injections of antitrypsin were among these fatalities. Of the 10 dogs, one died on the 2nd, 6 on the 3rd, and 2 on the 5th day, and one moribund animal was sacrificed on the 5th day after operation. Two of the dogs showed pronounced yellow discoloration of the liver, suggestive of toxic liver damage.

Of the remaining 9 dogs, one died on the 8th postoperative day of pneumonia and peritonitis without any fat necrosis. The other 8 animals were sacrificed, 4 on the 7th, 1 on the 21st, 1 on the 44th, 1 on the 54th, and 1 on the 88th day after the operation. Two of these animals showed a few insignificant fat necroses in the pancreas. The other 6 did not show any intraperitoneal disease.

Discussion

In the previous experiments, 16 out of 20 dogs (80 per cent) had died of extensive fat necrosis and only 20 per cent had survived. With the use of soybean antitrypsin, only 10 out of 19 dogs (52.6 per cent) died of fat necrosis while 47.4 per cent did not die of fat necrosis. The decrease of the mortality rate from 80 per cent to 52.6 per cent is too small to prove the value of trypsin inhibitor, though it may suggest some therapeutic effect. However, the decrease in mortality rate is of questionable statistical significance (chi square test). We discontinued experiments with soybean antitrypsin because the fatal results in 2 dogs with repeated injections of this substance and the signs of liver damage in 2 dogs made it appear that this preparation was toxic and that it was inadvisable to use larger doses. Other enzyme inhibitors may be less toxic and more effective.

Summary

An experimental procedure has been described previously which leads to fatal pancreatic fat necrosis in a high percentage of cases, and which seems to be suitable for the evaluation of prophylactic and therapeutic measures in this condition.

This is a report on the local use of soybean antitrypsin to prevent the development of pancreatic fat necrosis. Though there seemed to be some effect as far as the mortality rate was concerned, the results were not consistent enough to warrant continuation of these experiments.

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HYPERPLASTIC TUBERCULOSIS OF THE RECTUM*

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Hyperplastic tuberculosis is one of the rare lesions occasionally found in the rectum. It was first described in detail by Hartman and Pilliet in 1891. A perusal of the pertinent literature shows that all authors are agreed on its infrequency. However, one fact should be taken into consideration. Namely, that the likeness of this tumor to other hyperplastic, tumerous lesions of the rectum is so manifest that it is very readily confused with a hyperplasia of different genesis —most commonly with carcinoma. Its gross morphology and its symptomatology are so closely akin to carcinoma, that confusion is very possible if every means of diagnosis has not been exhausted. Therefore, we might conjecture that the infrequency of its discovery and reporting may be due partly to incomplete examination and hence faultily applied treatment of another disease, usually carcinoma. Other hyperplastic diseases to be commonly differentiated are: Lymphogranuloma venereum; gonorrheaic and syphilitic reactions; Hodgkin's disease; ameboma; actinomycosis; nonspecific foreign body granuloma; and a singular rectal lesion of a chronic regional ileitis.

The hyperplastic form of tuberculosis, also called "tuberculoma" by Herrick, is not quite so rare in other segments of the colon. The area of predilection is the cecum with the valvula Bauhini and the adjoining portion of the ileum as the most frequent site. There is no apparent reason for the predisposition of this intestinal structure. Hyperplastic tuberculosis may involve, however, any part of the large intestine, either in single or in multiple lesions, in rare cases even affecting the entire colon in the form of a tubular lesion.

Stenosis and stricture formation is not uncommon, as is secondary achalasia of the uninvolved adjoining proximal portion of the gut. Gabriel cautions one that a considerable reserve be exercised in assigning any importance to tuberculosis (and for that matter also to dysentery) in the production of rectal strictures, as these infections may precede or follow the acquisition of lymphogranuloma inguinale**. He states that the finding of acid-fast bacilli in material obtained from a rectal stricture does not necessarily prove the stricture to be of tuberculous origin.

In hyperplastic tuberculosis the mucous membrane is in many cases quite intact and there is usually no sign of ulceration, in contrast to the ulcerative variety of intestinal tuberculosis, which occurs with much greater frequency as compared with the hyperplastic type.

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*Presented at the meeting of the New York Proctologic Society on 10 April 1952.

†From the Department of Proctology of the New York Polyclinic Medical School and Hospital, New York, New York.

**In the American nomenclature: Lymphogranuloma venereum.

The ulcerative type of intestinal tuberculosis is considered secondary to other primary lesions of the system, chiefly of the lungs. In contrast, the hyperplastic type is recognized by many authors as a primary affection. They suggest that the causative organism is a less virulent bacillus Koch of a human strain or a bovine strain, which attacks the bowel directly through alimentary invasion while there is a possible vascular or/and alimentary spread in the ulcerative disease. Abscess, fistula, and peritonitis are uncommon in the hyperplastic type (Lockhart-Mummery).

In addition to the primary tumor, pedunculated or sessile polypoid or papillomatous outgrowths are found. They appear as small to hazel-nut sized elevations of firm consistency.

The symptoms caused by hyperplastic tuberculosis of the rectum are similar as for cancer, as heretofore mentioned. Superficial investigation will tend to result in faulty diagnosis of this more common disease.

The diagnosis is arrived at by digital and proctoscopic examination; demonstration of Koch bacillus; biopsy; and guinea pig innoculation with tissue. The value of these two laboratory procedures is divergently evaluated by various authors. E. G. Fannsler and Potter consider the microscopic method as the most valuable and not subject to the possibility of error. Sweany admits, in contrast, that granulation tissue of any chronic nature may simulate tuberculosis. The microscopic picture found is that of tuberculous granulation tissue with Langhans' type of giant cells, characteristic tubercle formation and necrotic center, fibroplastic capsule, and monocytic and lymphocytic infiltration. On the other hand, Martin, Lansford, and Sweany found guinea pig innoculation negative in 69 per cent and positive in 30 per cent.

The treatment of hyperplastic tuberculosis has undergone some change since the introduction of the antibiotics. But a few years ago, many authors stated that surgery was the only proper remedy for this condition, and to the same extent as for cancer. We attempt to show in the following case report that we have made good progress with streptomycin therapy.

Case Report

The patient is a fifty year old white male of Scandinavian nationality and residence. His profession, very appropriately, is skipper of a Scandinavian boat. He is married. His wife is healthy. One son is also healthy. One daughter has been suffering relapses of chronic bronchitis. Koch bacilli were never found in her sputum. The patient has lost two brothers in World War II. Other sisters and brothers are alive and healthy, though two of them are overweight. His father died from a heart attack, aged 58. His mother died from a cancer of the liver when 72.

The patient himself never underwent any surgery. In 1917, while in Holland, he had a hard chancre. Three weeks later, in Baltimore, he received three courses

of treatment with salvarsan. Wassermann was never positive, thereafter. In 1926 he was prone to repeated incidences of colds and coughs but tuberculosis was never found. In 1940 he began to suffer from bronchitis which ever since flares up when he has a cold. In 1943, while coming ashore in New York, he felt run-down and was examined in a prominent hospital of this city where a tuberculous spot in his right lung was established. His appetite was poor, but he was not running any temperature. There was no perspiration or diarrhea. Upon resting for some period of time he gained some weight back to his normal 70 kg. which he had been holding for the past twenty years. After 1943 he had a semi-annual checkup including x-ray with a chest specialist in Norway but no more active lesions were found.

His present condition began mid-February, 1951, on board ship. While sliding over the side-board of his bed, or when sitting on a beam he felt a pressure or the sensation of a foreign body in the rectum; also he had paresthesias of the

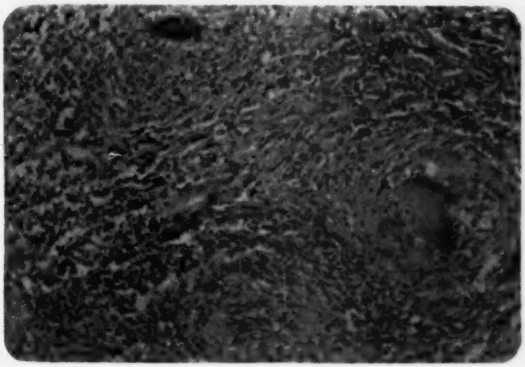

Fig. 1—Histopathologic specimen from the principal lesion shows characteristic tuberculous granulation tissue. In this picture there are virtually three tubercles shown, each respectively centered around a Langhans' giant cell with caseous focus, peripheral nuclei (horseshoe) and epitheloid cells, delicate reticulum, and a peripheral rim of lymphocytes.

perirectal area especially when sitting a long time. When he felt tired the sensation was more pronounced, also when he was constipated. Depending on the type of food he ate there had been a tendency to constipation all his life. This pressure sensation gradually grew worse but there was never real pain. There was no radiation of this sensation. Relief came after bowel movement and there was complete disappearance of this sensation after thorough evacuation with laxatives for a day or two.

On March 15, he landed in New Orleans and visited a doctor who, after examination, told him that he had a rectal carcinoma. He admitted him to a well-known hospital there, where a prominent specialist saw him and took a biopsy. The same evening the specialist cancelled the diagnosis of carcinoma and

repeated the biopsy a specimen of which was sent to four different institutions in the United States, one of which was a leading hospital in New York City. One hour after the second biopsy the patient began to hemorrhage severely and received two pints of serum and two pints of whole blood. The report of the biopsy from the New York institution confirming the other reports reads as follows: ". . . the lesion seen in this section is certainly consistent with tuberculosis. Proof, of course, will depend on demonstrating the presence of tubercle bacilli." A few days later, after a Frei test and blood serology had proved negative and a complete blood count and sedimentation rate were within normal limits, the patient was put on the regime of 0.5 gm. of dihydrostreptomycin twice daily.

Four weeks later the patient moved on to New York City. Examination here revealed an annular lesion about 8 cm. ab ano. The lesion appeared and felt indurated, with a fine granular surface. It was situated at the crest of a valve extending about 12-15 mm. proximo-distally. Its color was whitish-gray and there was a proximal lining zone of red hemorrhagic border. There was some moderate stricture of the lumen which, however, failed to block it effectively. There was one elevation of about the size of a pea within the area of the lesion. There were some more singular lesions unattached to the mother lesion: small dome-shaped, round elevations of 1-4 mm. diameter distally on the anterior rectal wall.

Because of the rarity of this lesion and its proctologic interest, the case was presented to Dr. R. V. Gorsch, at the New York Polyclinic Hospital in New York, who verified the diagnosis and demonstrated the case to a group of postgraduate students and also took a biopsy for guinea pig inoculation, which proved to be negative for tuberculosis after three months had elapsed. Kodachrome pictures of the lesion were taken but unfortunately never became available. The original histopathologic slide of the biopsy specimen was obtained and micro-Kodachrome photography was performed through courtesy of the pathologic laboratory of the Long Island College Hospital in Brooklyn, New York. The microscopic picture which is consistent with tuberculosis is being presented here (Fig. 1).

Summary

A hyperplastic tuberculous lesion of the rectum is being presented which is considered a rarity.

There are a few criteria which may deserve discussion. Here is a man who as a professional merchant mariner travels about the world including tropical countries. There is a syphilitic infection in his medical history. Any of the hyperplastic lesions as mentioned in the introduction had to be considered. Carcinoma would have a different pathohistological appearance and clinical course; lymphogranuloma venereum was ruled out by a negative Frei test; a syphilitic hyperplasia would offer a different microscopic picture; there was a lack of the clinical picture and findings of Hodgkin's disease and of amebiasis. There was no reason to presume the presence of a localized rectal lesion of chronic regional

ileitis or of a foreign body granuloma. Thus, even in the absence of proof by guinea pig inoculation—the value of a negative result of which is held questionable by a group of authors—the diagnosis of tuberculosis could be established by histologic affirmation.

Another angle to be mentioned is the fact that this case failed to corroborate the general claim that hyperplastic tuberculosis of the intestines is a primary disease. This patient had a positive pulmonary tuberculous infection previously. It should also be noted that taking a biopsy from these cases may elicit severe hemorrhage. Furthermore, the therapeutic effect of modern antibiotics offers a remarkable progress also in the treatment of intestinal tuberculosis, considering that not yet antiquated textbooks and papers are agreed upon the necessity of surgery for hyperplastic tuberculosis and to the same extent as for carcinoma. And for that matter, it remains to be seen whether the new anti-TB drugs, Marsilid and Nydrazid, will render even more dramatic results.

Our patient has shown to benefit materially from the treatment with daily injections of dihydrostreptomycin which were continued during his stay at this city. The lesion became visibly smaller and the pea-sized elevation could be observed to shrink within a few weeks. Moreover, the patient felt perfectly well again and his initial symptoms of rectal pressure had disappeared entirely.

Discussion

Dr. Isaac Skir (*Brooklyn, N. Y.*):—Hyperplastic or hypertrophic tuberculosis, or as some would have it, tuberculoma, is a rare occurrence, but when found in the rectum it is somewhat of a curiosity. Bargen, Yeomans, Lithicum and Jelks each reported one case. During the eighteen years that I have been on the Tuberculosis Service of the Kingston Avenue Hospital, we have seen no rectal tuberculomas. However, at the same hospital, just prior to this period, A. W. Martin Marino listed an operation for a "tuberculoma of the rectum", though the pathological report called it simply "tuberculosis". Many other observers of wide experience among the tuberculous have failed to encounter this condition.

It is not unlikely, of course, that some cases have gone unrecognized or, at least, unreported. Errors in diagnosis are likely. Clement Martin points out that in some cases of hyperplastic tuberculosis tubercles may be so scarce that they are missed in many sections. Thus, in a case cited by Mouat (1925) a positive guinea pig test was obtained in spite of a negative histological report. One wonders how often tuberculomas have been treated as carcinomas.

On the other hand it is, at times, difficult to positively identify a structure as hypertrophic tuberculosis. Some of our most outstanding pathologists have been known to disagree as to whether a certain lesion was tubercular or cancerous. Other conditions which may confound us are ameboma, gumma, sarcoma, Hodgkin's, lymphoma, sarcoid, actinomycosis, venereal lymphogranuloma, and regional proctitis.

The great majority of patients with hyperplastic tuberculosis of the large intestine have no tuberculosis elsewhere in the body. May this process possibly be due to an organism different from the usual strains of tuberculosis? Or is it due to a mixed infection, to attenuated virulence of the organism, or to exceptionally high resistance of the host?

With the advent of the newer tuberculocides, we may perhaps hope that we may be able to apply therapeutic tests so as to obviate the necessity for surgery in some cases.

Dr. Vogel is to be congratulated for calling our attention to this very rare and interesting condition, and to the necessity for circumspection in the diagnosis of rectal tumors.

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ATHEROSCLEROSIS

I. The Monolayer Theory

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Introduction

For over 400 years, scientists have been studying the problem of atherosclerosis and in the interval have accumulated a vast body of information. The lack of an adequate theory integrating this collection of unrelated facts has resulted in many inconsistencies.

The current situation has been succinctly and adequately summarized by Duff and McMillan[1], who state: "Almost nothing is known of the means by which lipids enter the arterial intima or how they become fixed there . . . the clear recognition and understanding of all the factors concerned in the etiology and pathogenesis of arteriosclerosis must await the future." Hence, before we can embark upon a rational program directed toward the prevention of arteriosclerosis, the mechanism underlying the process must be uncovered.

The following is concerned with a theory which may explain the mechanism of lipid deposition, and provide a means for attacking the problem. It will also correlate several of the other proposed theories which are contributory but insufficient by themselves. While the theory herein proposed awaits further experimental verification, it permits of sufficient application to warrant the consideration of all investigators concerned with the problem.

The formulation of this theory is based on established facts gathered from the study of monomolecular layers (monolayers), and is applied in conjunction with basic principles derived from the science of fluid dynamics.

The Theory

By definition, the monolayer is a film, one molecule in thickness, composed of all the constituents which are present in the fluid portion of the blood with the exception of the blood cells. The production of atherosclerosis is mediated through this postulated monolayer. The monolayer is in intimate contact with

This work was aided by a grant from the Commercial Solvents Co., New York, N. Y.
A contribution from the Geriatrics Institute, division of the Home and Hospital of the Daughters of Jacob, Bronx 56, N. Y.

the walls of the vascular system and the blood stream. The presence of the monolayer is determined by local hemodynamic conditions – primarily the stream velocity. The extent of the monolayer, i.e., the area which it occupies, is also a function of the stream velocity – increasing as the stream velocity increases. The state of the monolayer is in dynamic equilibrium with and conditioned by the chemical and physical properties of the blood.

The Science of Monolayers

The study of monolayers has been developing rapidly in recent years and while its technics have not been too widely applied, biologists, cytologists and physical chemists are displaying an increasing interest in this method of investigation. Cellular physiologists have recently found the monolayer technic most productive in yielding information on the properties of cell membranes aproximately a molecule in thickness and composed of lipoproteins[2].

Monolayers composed of fatty acids, oils or proteins may be readily studied with the aid of the film balance, a sensitive instrument used in recording small changes of surface pressure. By spreading these substances on a clean, polar surface such as water, the physical state of the formed film is determinable by measuring its surface viscosity, surface potential and surface pressure. It has been demonstrated that for a given monolayer a progressive increase of applied surface pressure will alter its physical state from that of a gas to a liquid and finally to that of a solid (Fig. 1). This increased surface pressure is brought about by decreasing the area the film occupies and thus bringing the molecules into closer proximity. Conversely, a progressive decrease in applied presure will result in a complete reversal of events. Moreover, these changes in state are conditioned by the duration of applied pressure; e. g., if a monolayer is maintained in the solid phase for an extended period of time it a) becomes irreversibly solidified, or b) there may be a time lag in the return of the film to its original gaseous state as the pressure is progressively decreased. This latter phenomenon is designated as hysteresis.

Certain established principles and facts[2,3] derived from the study of monolayers will be employed to explain the formation of atherosclerosis and its varied manifestations in terms of the Monolayer Theory.

The energy of association between molecules when they are adlineated at an interface can be of the order of 30,000 cal. which is more than sufficient to change the chemical and, more important, the biological activity of the compound.

As soon as the energy of the associating forces between the molecules commences to predominate over their kinetic energy, the monolayer will change its state.

Adlineation between large molecules lying on the surface at high surface compression is probably responsible for the formation of gels and films of high viscosity.

This film is reversible except when it is held for any length of time at high pressure.

Compounds that penetrate cholesterol monolayers or disperse protein films are usually also hemolytic.

Interfacial films readily become rigid or elastic under some circumstances.

Sterol films are penetrated by the hemolytic glucosides saponin and digitonin; and by bilirubin and the capillary active porphyrins.

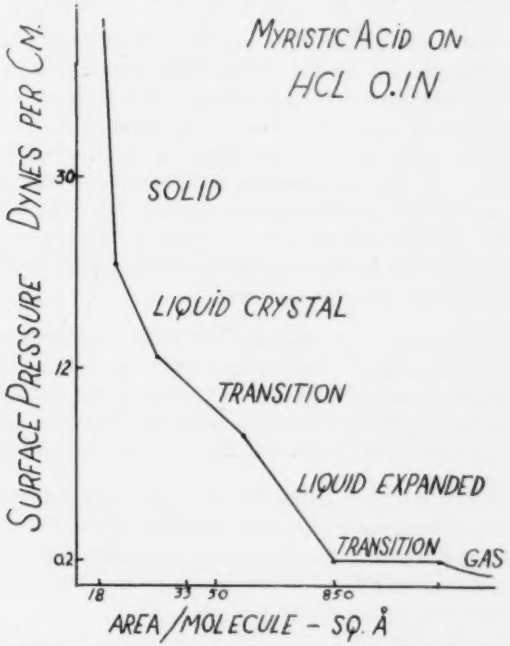

Fig. 1—Schematic. Changes in state of a typical monomolecular layer from a gas to a liquid to a solid, and transition zones, as the area/molecule is decreased. Decrease in area/molecule can also be accomplished by increasing the number of molecules and maintaining the total area constant.

The adsorption of metallic ions, which in minute quantities may profoundly affect the properties of monolayers has been studied – the di-valent ions such as calcium are able, in occupying two or more end groups to confer considerable rigidity.

Condensation of films tends to be abolished by high temperatures and by the presence of double bonds or of particular substituents in the steroid nucleus.

Fluid Dynamics and The Monolayer

In any tubular system through which a fluid is being transported, the characteristics of the flow will be conditioned primarily by the pressure, the diameter and length of the tube, and the viscosity and density of the conducted fluid. There are two types of flow which are determined by the velocity. Above a certain critical velocity there is turbulence (turbulent flow) while below this critical velocity there is an absence of turbulence (laminar flow). In laminar flow the fluid moves in concentric layers with each layer traveling at a different velocity. At the stream center the relative velocity is most rapid. Proceeding from the center toward the wall of the tube, the velocity diminishes and at the wall it is practically zero (Fig. 2)[4,7].

While this variation in fluid flow has been known for a very long time, it has not been generally appreciated. Poiseuille[5] commenting in his memoirs on the movement of blood, noted an exceedingly thin stagnant layer at the walls of the containing vessel. Since this observation, workers in fluid dynamics have devoted much time to the study of the liquid layer adjacent to a solid surface. Fage and Towend[6] in their examination with an ultramicroscope of the solid-liquid boundary observed that the slowest particle had a mean velocity of 0.006 ft./sec. when the average velocity across a section of the tube was 0.83 ft./sec. It was calculated that this particle would be at an infinitesimally small distance of about 0.0000625 mm. from the surface.

In their discussion of heat transfer, chemical engineers have contributed further pertinent information[7]. They assume that the surface film of a fluid is of a definite though unknown thickness. By reducing the thickness of the boundary layer, optimum conditions for heat transfer are obtained. Other things being equal, this is brought about by increasing the fluid velocity past the surface.

Experimentally it has been found that in a rigid conducting system the thickness of the surface film is an exponential function of the velocity and inversely proportional to this function, whereas for an oscillating system the thickness of the boundary layer is proportional to the square roots of the product of the Kinematic viscosity and the period of the motion[8].

In general, boundary layers are formed whenever a fluid of low viscosity flows past a solid surface. They are also formed in the inlet lengths of tubes. With certain types of entry (such as a trumpet shape or non-sharp orifice) the flow is uniform over a cross-section. Later the fluid near the walls is retarded. In laminar flow, the retarded layer grows in thickness in proportion to the square root of the distance from the entry[9].

Since the existence of this fluid film adjacent to the wall of the conducting tube is dependent on the stream velocity, we shall list those factors which affect the velocity.

1) The greater the pressure gradient of the transported fluid the greater its velocity.
2) For a given pressure gradient – a decrease in the cross-sectional area of the conducting tube will increase the velocity of flow.
3) An increase in the density of the fluid will increase the velocity.
4) A decrease in viscosity will increase the velocity.

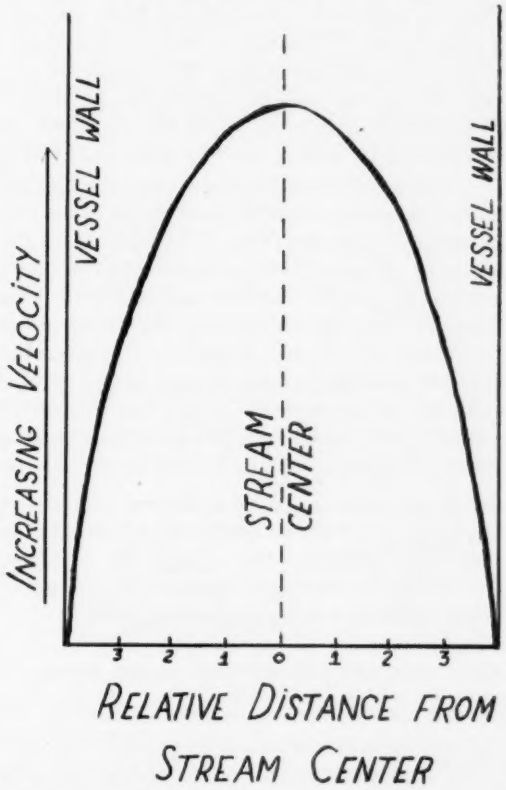

Fig. 2—Diagram illustrating the relative distribution of velocities in a section of a conducting vessel in which the flow is laminar. The velocity is relatively greatest at the center and least at the wall of the vessel.

Application of the Monolayer Theory

The Monolayer Theory will be applied from two broad aspects; the physical and the chemical factors which control its existence and state. Velocity of the fluid stream conditions the site of monolayer formation and will be employed in explaining the morphological manifestations of lipid deposition, whereas the

chemical factors participate in the acceleration or inhibition of lipid deposition insofar as they help to rigidify or disperse monolayers.

The Mechanism of Lipid Deposition in the Vascular Walls

It is generally agreed that there is a relationship between the lipid quality and quantity of the serum bathing the vascular wall and the incidence and severity of atherosclerosis – a high serum level of lipid being conducive to deposition and a low serum level having a diminishing effect. While these lipid molecules are coursing through the circulatory system, their kinetic energy and the intermolecular collisions with themselves and other molecules prevent their combining and being thrown out of solution. Near the surface of the conducting vessel, however, these molecules form part of the film layer and their kinetic energy is reduced. Normally, these components leave and enter the film layer through processes of diffusion. An increased concentration of lipids in the serum will result in an increased concentration in the film. Now, if the thickness of the film is reduced to that of a monolayer by an increase of stream velocity, the energy of association will begin to predominate (supra) and the molecules will become adherent to each other. This increase in size by combination will further decrease diffusibility into the blood stream from the film and, if delayed, the molecular aggregates will become more adherent, grow larger and in time form a rigid irreversible film. This occurs sporadically or continuously with a cumulative effect resulting in atherosclerotic changes of the vessel wall. The area these films occupy need not necessarily be extensive, although the area will be larger with increased velocity.

It may be several molecules in extent or several centimeters, depending on the intensity and duration of the factors contributing to film formation—e.g., local stream velocity, lipid concentration. Once a rigid film is formed it may be absorbed through the endothelium or it may remain fixed at the site of its formation with perhaps a slight amount of "creeping" taking place.

Confinement of Deposition to the Arteries

In most instances lipid deposition is restricted to the arteries, while the lymphatic and venous systems are spared. Moschowitz[10] attributes this selectivity to a concomitant higher arterial pressure gradient and cites abundant evidence to substantiate his contention. However, his hypothesis fails to account for the slight deposition normally occurring at such low pressure sites as the junction of the iliac veins with the vena cava[10] and at the entrance to the right auricle[11] – a point in the circulation which is almost at zero pressure. It is readily apparent therefore that there is another factor which, though it is potentiated by pressure, is responsible for affecting deposition.

It is well known that the variations in velocity throughout the vascular system are quite different from those of pressure. The velocity is high in the arteries but is reduced several hundred times in the capillaries and small veins (Fig. 3).

There is a subsequent rise in the larger veins, where the velocity approaches but rarely reaches the arterial rate. Pressure on the other hand, falls continuously as the blood flows through the arteries, the capillaries and finally the veins.

Absolute values for stream velocity in the circulatory system are very scant. Until the time that such information becomes available, much of it will have to be deduced from fluid dynamic principles. Some measurements, however, have been made. For example, it has been found that in the larger arteries of the dog during rest, the velocity is from 0.1 to 0.2 meters/sec., in the capillaries about 0.5 mm./sec., and in the medium sized and large veins from 0.06 to 0.2 meters/sec. By indirect measurement, velocity in the human aorta has been found to be around 0.4 meters/sec. during bodily rest and during strenuous exercise, when the output of the heart is large (20 liters/min.) the velocity is over 2 meters/sec. — a five-fold increase.

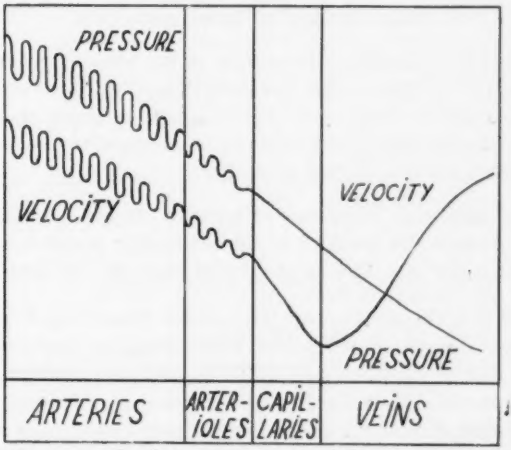

Fig. 3—Schematic. Pressure and velocity variations in different parts of the vascular system. Pressure continuously decreases and approaches zero, while velocity continuously declines from the arteries to the capillaries but, in the veins, starts to increase and approaches in magnitude the velocity of the blood in the arteries.

It is to the velocity gradient that we attribute lipid deposition. Pressure is significant only insofar as it affects velocity. On the arterial side the two variables, D (diameter) and V (velocity), favor monolayer formation. An increased demand on the carrying capacity of the aorta is met by a greatly increased flow rate or velocity and only a slight increase in aortic diameter because of its rather small distensibility — about 20 per cent.

While the quantity of blood transported by the aorta must be equalled in extent by the vena cava, adaptation is of a different kind. Instead of increasing its velocity of blood flow, the vena cava increases its diameter due to its greater distensibility which is about 60 per cent (Fig. 4). This accommodation to increased

demand in its carrying capacity tends to prevent any great increase in stream velocity and is characteristic of the entire venous system. Hence, monolayer formation is not favored in the venous system and accounts for the normal absence of lipid deposits. It is of interest to note that there is a progressive decrease in pressure in the venous system from the periphery to the heart – yet, at the point of zero pressure at the entrance to the right auricle, lipid deposition has been observed. Furthermore, at this point the vena cava is the least distensible (contains more muscular tissue) and the venous velocity is the highest.

Lipid deposition in the lymphatic system is practically unknown, despite the fact that it is subjected to a great load of lipid during absorption[12]. This is readily explained in terms of the Monolayer Theory. Lymphatic flow is sluggish and there is very little chance of monolayer formation taking place.

Localization of Lipid Deposition

The phenomena of localized deposition in the arterial system is another aspect of atherosclerosis wherein the "pressure theory" finds difficulties of explanation. If these localization effects were due mainly to pressure, sharp differences in pressure would have to exist side-by-side or be confined to one side of a vessel – a situation which leads to a logical absurdity.

Bearing in mind that increased velocity of stream flow favors monolayer formation and permits the energies of intermolecular association to exert themselves, let us focus our attention on these preferred sites of deposition.

In addition to a predilection for the arterial system, lipids exhibit a preferential sequence of deposition. It has long been noted that deposition is frequently initiated at the root of the aorta and gradually and progressively involves the remainder of the vessel. While the thoracic segment of the aorta, along with the root, is involved first, in time the abdominal segment shows more extensive lesions. Other sites of marked deposition are the arch of the aorta and the entrances to the intercostal and iliac arteries. This morphology and sequential deposition is understandable within the framework of the Monolayer Theory.

We have mentioned above that with certain types of entry, such as a trumpet shape or non-sharp orifice, the flow when it enters the conducting vessel is uniform over a cross-section. Later the fluid near the walls is retarded and grows in thickness. Other things being equal, this means that the boundary layer tends to be thinnest at a point of entry, and as a result is a preferred site of monolayer formation. It follows that deposition will be most prominent at the beginning or mouth of an artery and is substantiated by observation. This also accounts for deposition at the root of the aorta. A slight decrease in diameter occurs in the aortic arch which increases the stream velocity over this region. This, along with the fact that the velocity of flow is displaced toward the outer wall in a curved conduit, accounts for the deposition in the aortic arch especially on its greater curva-

ture. With time there is a further displacement of stream velocity in the aorta. The thoracic segment becomes dilated and results in a relative narrowing of the abdominal section. Because of this relative reduction in cross-section the velocity will be correspondingly elevated, and accounts for the noticeable intensification of the atherosclerotic processes in the abdominal aorta. This has been well demonstrated in autopsy cases when the thoracic segment and aortic root were found to be enormously dilated and singularly unmarked while the abdominal segment exhibited profuse deposition.

Composition of Deposits

There is very little doubt that the material deposited in an atheromatous vessel originates from the blood stream directly bathing the vessel wall. Numerous chemical analyses have shown these plaques to consist of cholesterol, cholesterol esters, glycerol esters and calcium, all normal components of blood. A further com-

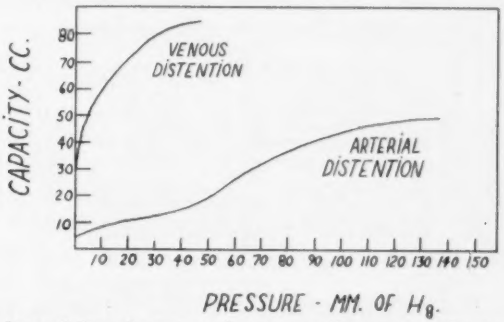

Fig. 4—Curves of distensibility of a vein and an artery. Figures on ordinate represent capacity of a section of a vessel when distended by pressure (abscissa).

ponent found in the plaques is dihydrocholesterol[13]. This appears to the extent of about 10 per cent of the total cholesterol in the plaques and is much more than that found in any other part of the body. Also noteworthy, is the absence in the plaques of unsaturated sterols such as the estrogens. Although the composition has thus been determined, no general explanation has been advanced to account for these constituents. The Monolayer Theory provides an explanation.

In a given region where velocity factors are favorable for the thinning of the boundary layer, the lipid components and calcium will accumulate due to a loss in kinetic energy, as shown in the discussion of the mechanism of deposition. If steroids with an unsaturated nucleus are present, film condensation will be aborted and the components dispersed (supra). This has been repeatedly demonstrated in experimental studies of monolayers[3]. The dispersing effect is counterbalanced to some extent by the tendency of calcium (a di-valent-ion) to confer rigidity upon the film (supra). A dynamic equilibrium is thus established — the point of equilibrium shifting to favor deposition as the concentration of unsatur-

ated steroids is reduced, or the concentration of the saturated steroids is increased. Again it is to be emphasized, this may occur sporadically or continuously, but ultimately there will be a cumulative effect (Fig. 5).

Instances of Acceleration and Inhibition of Atherosclerosis

We have shown in the preceding section how regional velocity differences provide a rationale for the morphology of lipid deposition. In this section we shall explain why the atherosclerotic process is intensified in certain conditions while in others it is suppressed.

In diabetes, nephrosis, familial hypercholesterolemia, hyperlipemia, hypothyroidism, xanthomatosis there is a marked elevation of serum lipids particularly cholesterol. This is paralleled by an increased concentration in the monolayer,

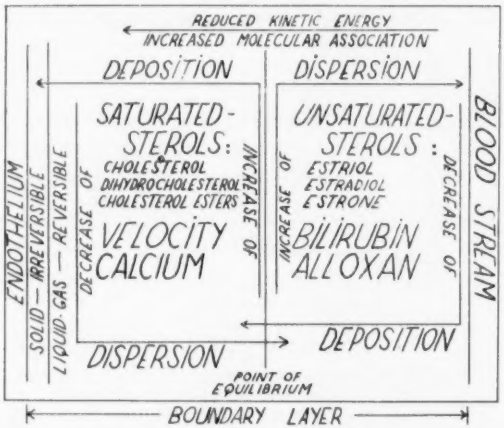

Fig. 5—Equilibrium Diagram. Illustrating how various factors can combine to shift the point of equilibrium toward or away from deposition.

and results in an unbalanced equilibrium and a shift in the direction of deposition. In other words, in these disease states there is an exaggeration and acceleration of the processes normally occurring in the monolayer simply due to an increased increment of lipids.

In hypertension, both generalized and local, disequilibrium again occurs and will result in intensified deposition. Since pressure is significant only insofar as it increases velocity, a persistently elevated pressure will result in a sustained elevated velocity. This will predispose to greater lipid deposition since more extensive monolayer formation will occur.

With an elevated serum lipid level and a superimposed increase in stream velocity, conditions should be theoretically ideal for the acceleration of the atherosclerotic process.

The incidence and severity of atherosclerosis are noted to be much greater in the male than in the female. In the absence of disease this has been attributed to the differences in sex hormones. Moreover, it is noted that during the child-bearing period lipid deposition is even further decreased, while in the menopausal period there is an intensification. This is in contrast to the situation in the male where the involvement is progressive and without periods of abatement. Again, these variations are consistent and understandable in the light of the Monolayer Theory. It will be recalled that the female hormones estrone, estriol and estradiol contain an unsaturated portion in their nucleus in ring I of conjugated double bonds, whereas the male hormones testosterone and androsterone do not. It has been demonstrated that steroids containing double bond systems are able to exert a dispersing effect on sterol and protein monolayers. This fact, in conjunction with the tendency of the female in the child-bearing years to have a decreased blood calcium level, shifts the monolayer equilibrium in the direction away from deposition. The effectiveness of this film dispersing mechanism is diminished

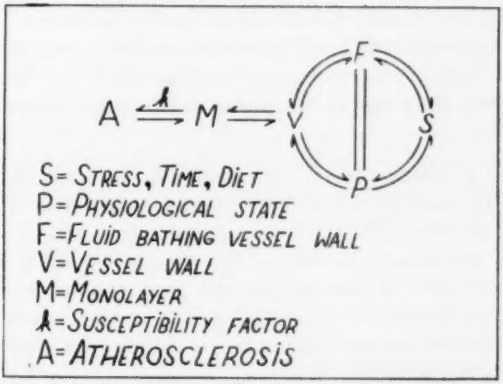

Fig. 6—Symbolization of atherosclerotic processes determined by factors operating in an equilibrium cycle. *k* will vary from individual to individual and from species to species and should be calculable — thus serving as an index of an organism as to its susceptibility to the atherosclerotic process.

in the postmenopause when there is a great decrease in the secretion of estrogens and the atherosclerotic process is intensified — the equilibrium then shifts in the monolayer in the direction toward deposition.

Bilirubin exerts a dispersing effect on monolayer films (supra). It is predicted therefore that those individuals with a prolonged elevation of bilirubin levels will have a lowered incidence of atherosclerosis. This, too, may account for the decreased incidence of lipid deposits in chronic alcoholics who often have an accompanying liver dysfunction and elevated serum bilirubin levels. Further, estrogens are known to be metabolized in the liver. If this degradation of the molecule is blocked, estrogens will accumulate in the blood and an additional protective effect will be exerted.

In xanthomatosis, lipid levels are elevated tremendously and there is widespread deposition in the vascular walls. However, when this is accompanied with primary biliary cirrhosis, no deposition in the vascular walls occurs. This is now understandable. Deposition cannot occur because of the dispersing effect of bilirubin on the monolayer.

Finally, we cite one further bit of evidence which lends substantiation to the Monolayer Theory. If an animal is made diabetic with alloxan and then fed cholesterol, the serum cholesterol levels will rise tremendously but deposition in the vessel will be inhibited[14]. Alloxan, in addition to its diabetogenic action is a hemolytic agent and causes profound hemolysis[15, 16].

The whole complex problem of lipid deposition can be symbolized in terms of an equilibrium cycle. Any disequilibriating effect leads to deposition (Fig. 6).

Discussion

The complete presentation here is almost wholly theoretical and requires extensive experimental verification. We have refrained from presenting the rigorous analysis of the problem of atherosclerosis which has led to the Monolayer Theory, since it is not within the scope of this paper and is being further developed and extended[17].

Conditions at a boundary layer on a molecular level are still in the process of elucidation[18]. The fact that fluid flow is laminar, that each layer travels at a diminishing rate, as the wall of the vessel is approached, led by extension to the postulation of the monolayer. The role of the stream velocity in determining the existence of a monolayer is indicated by the experimental results of chemical engineers and investigators in fluid dynamics. The chemical factors conditioning the film state, condensation or dispersion, are amply substantiated by investigative work on monomolecular layers.

Application of the Monolayer Theory has permitted the formulation of a mechanism for deposition. It has also resulted in the integration of previously unrelated factual material, and has indicated the limitation of other theories.

Experimental work testing critical portions of the theory herein presented are now in progress at the authors' laboratories. A detailed mapping of sites of lipid deposition, and their relation to vessel diameter and the physical and chemical factors concerned with them will soon be completed[19]. *In vitro* studies on sterol and lipoprotein monolayers employing the monolayer technic and the effects of estrogens, androgens, alloxan, thyroxine, and various nontoxic derivatives of these on film dispersion are also being instituted[20]. Clinical and animal studies aimed at correlating the degree and incidence of atherosclerosis with the physiological and biochemical factors affecting monolayers in certain disease states are also being projected[21]. Similar studies concerned with the factor of aging are also being undertaken[22].

The implications of the work presented here are evident. A considerable clarification of the obscurities of atherosclerosis has been obtained and a fresh point of attack on the problem is provided that is readily amenable to experimentation.

Recently, the emphasis in the investigation of atherosclerosis has been on the detailing of the chemical composition of the lipids of the blood, with the exception of Moschowitz. We hope that this presentation of the Monolayer Theory will redirect the energies of investigators toward the elucidation of the physical factors involved in this age-old – "old-age" problem.

SUMMARY

A new theory is presented which provides a rationale for the formation of atherosclerosis on the basis of a postulated monolayer, and known principles of fluid dynamics.

The velocity of the fluid stream conditions the site of monolayer formation and explains the morphological manifestations of lipid deposition.

Chemical factors participate in deposition of lipid by condensing or dispersing the components of monolayers.

The Monolayer Theory serves to explain and integrate previously unrelated factual material such as the role of pressure, lipid levels, sex differences, localization of deposition, and restriction of atherosclerosis to the arterial system.

Since monolayers are readily amenable to *in vitro* experimentation, it is conceivable that effective, nontoxic dispersing agents will be discovered which may eventually lead to the abolition of atherosclerosis.

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NEWS NOTES

Seventeenth Annual Convention

The program for our Seventeenth Annual Convention will be found in this issue of The Review of Gastroenterology.

Copies are being mailed out separately to members of the Association and additional programs are available from the headquarters office, 1819 Broadway, New York 23, N. Y. The program will also be available at the registration desk on the convention floor.

Featured this year will be a Symposium for the General Practitioner on Tuesday morning, 21 October 1952, at which problems of interest will be discussed.

The Wednesday evening session, which has proved to be popular, will again be continued.

The Convention sessions are open to the general medical public.

Registration

Those attending the convention are requested to register and receive their identification badges. Ladies are also invited to register. No one will be admitted to the exhibits or the sessions without a badge.

Annual Meeting of the National Council

The Annual Meeting of the National Council of the National Gastroenterological Association will be held at the Hotel Statler in New York, N. Y. on Sunday afternoon, 19 October 1952, at 4:00 P.M.

Following the meeting of the Council there will be a banquet for the officers and members of the Council.

Annual Meeting of the National Executive Committee

The Annual Meeting of the National Executive Committee will be held at the Hotel Statler in New York, N. Y., at 3:00 P.M. on Sunday afternoon, 19 October 1952.

Annual Meeting of the National Gastroenterological Association

The Annual Meeting of the National Gastroenterological Association will be held at the Hotel Statler in New York, N. Y., at 4:00 P.M. on Monday, 20 October 1952, the first day of the Seventeenth Annual Convention. Members of the Association are invited to attend and participate in the business meeting.

Program

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

SEVENTEENTH ANNUAL CONVENTION
20, 21, 22 OCTOBER 1952
and
COURSE IN POSTGRADUATE GASTROENTEROLOGY
23, 24, 25 OCTOBER 1952

HOTEL STATLER
Seventh Avenue and 33rd Street, New York, N. Y.

Members of the medical profession are cordially invited to attend the convention sessions.

Attendance at the Postgraduate Course is limited to those who have paid the matriculation fee.

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FRED H. VOSS, M.D.
Phoenicia, N. Y.
LESTER R. WHITAKER, M.D.
Portsmouth, N. H.

Executive Officer
DANIEL WEISS, B.S., M.A.

PROGRAM COMMITTEE

WILLIAM W. LERMANN, M.D., Chairman
1819 Broadway
New York 23, N. Y.

ANTHONY BASSLER, M.D.
New York, N. Y.
SIGURD W. JOHNSEN, M.D.
Passaic, N. J.
FRANZ J. LUST, M.D.
New York, N. Y.
C. J. TIDMARSH, M.D.
Montreal, Canada
ROY UPHAM, M.D.
New York, N. Y.
SAMUEL WEISS, M.D.
New York, N. Y.

REGISTRATION—All members and guests should register. Identification badges for admittance to meetings will be given to those who register. These should be worn at all times during the session. Registration will take place at the registration desk on the convention floor.

LADIES REGISTRATION—At the registration desk on the Convention Floor. Registration facilities will be open at 8:30 each morning. Information concerning the various activities and events will be available there.

MEETINGS are held on Eastern Standard Time and will begin promptly at the time specified.

COURSE IN POSTGRADUATE GASTROENTEROLOGY—Admittance only upon presentation of official matriculation card.

SCIENTIFIC EXHIBITS—Will be in the Exhibit Hall and will be open daily, Tuesday to Friday.

TECHNICAL EXHIBITS under the direction of Mr. Steven K. Herlitz, Exhibit Manager, will be open Tuesday to Friday.

Those attending the Convention are urged to take advantage of the time in between the presentation of papers and sessions, to visit the technical exhibits and become acquainted with the many new products and new equipment on display.

PROGRAM

SEVENTEENTH ANNUAL CONVENTION
NATIONAL GASTROENTEROLOGICAL ASSOCIATION

SCIENTIFIC SESSIONS
20, 21, 22 OCTOBER 1952

and

COURSE IN POSTGRADUATE GASTROENTEROLOGY
23, 24, 25 OCTOBER 1952

HOTEL STATLER

Seventh Avenue and 33rd Street

New York, N. Y.

SPEAKERS AND OFFICERS OF INSTRUCTION

ADLERSBERG, DAVID, M.D., Assistant Clinical Professor of Medicine, Columbia University, College of Physicians and Surgeons; Associate Physician, Beth Israel Hospital; Adjunct Physician for Metabolic Diseases, The Mt. Sinai Hospital, New York, N. Y.

BANCROFT, FREDERIC W., M.D., F.A.C.S., Professor of Clinical Surgery, New York Medical College, New York, N. Y.

BAROWSKY, HARRY, B.S., M.D., Assistant Professor of Clinical Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y.

BENDICK, ARTHUR J., M.D., Sc.D., Director, X-ray Department, Beth Israel Hospital; Consultant, X-ray, The Mt. Sinai and Montefiore Hospitals, New York, N. Y.

BERGER, ADOLPH, D.D.S., Professor Emeritus (William Carr) Oral Surgery, Columbia University; Faculty of Medicine; Consultant, Oral Surgery, Presbyterian, Beth Israel Hospitals and Hospital for Joint Diseases, New York, N. Y.

BERGER, SAMUEL S., M.D., F.A.C.P., Consultant in Medicine, in charge of Gastroenterology, Mt. Sinai Hospital, Cleveland, Ohio.

BOROS, EDWIN, M.D., Assistant Clinical Professor of Medicine, New York University-Postgraduate Medical School; Gastroenterologist, Bronx Hospital, New York, N. Y.

BOYD, LINN J., M.D., F.A.C.P., Director of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals; Metropolitan Hospital; Bird S. Coler Hospital, New York, N. Y.

CANTELLORS, JOSE M., B.S., M.D., Fellow in Surgery, Knickerbocker Hospital, New York, N. Y.

CAVE, HENRY, A.B., M.D., Clinical Professor of Surgery, Columbia University, College of Physicians and Surgeons; Chief, 1st Surgical Division, The Roosevelt Hospital, New York, N. Y.

CONNORS, R. J., Chief, Proctological Department, St. Anne's Hospital; Attending Proctologist, Fall River General Hospital, Fall River, Mass.

COOPER, WILLIAM A., A.B., M.D., F.A.C.S., Associate Professor of Clinical Surgery, Cornell University Medical College; Assistant Attending Surgeon, New York Hospital, New York, N. Y.

COWETT, MAX P., M.D., Assistant Professor of Surgery, New York University Medical School; Associate Visiting Surgeon, Chief Proctologist, Bellevue Hospital; Associate Attending Surgeon, University Hospital; Consulting Proctologist, St. John's Hospital, Yonkers, New York; Lecturer in Proctology, New York Polyclinic Medical School and Hospital, New York, N. Y.

VISIT THE EXHIBITS

DUBIN, I. N., Major, M.C., Chief of Hepatic Pathology Section and Registrar of the Hepatic Registry, American Registry of Pathology, Armed Forces Institute of Pathology, Washington, D. C.

ERF, L. A., M.D., B.S., Assistant Professor of Medicine, Jefferson Medical College and Hospital, Philadelphia, Pa.

FARRAND, ROBERT E., B.S., M.D., Teaching Fellow in Surgery, Harvard Medical School, Consultant in Thoracic Surgery, Waltham, Malden, Mt. Auburn Hospitals, Boston, Mass.

FINEMAN, SOL, B.S., M.A., M.B., M.D., Associate Clinical Professor of Radiology, Columbia University, College of Physicians and Surgeons; Attending Roentgenologist, Montefiore Hospital, New York, N. Y.

FIORETTI, CARLO, B.S., M.D., Senior Surgeon, St. Bernard Hospital, Chicago, Ill.

FLOOD, CHARLES A., M.D., Assistant Clinical Professor of Medicine, Columbia University, College of Physicians and Surgeons, New York, N. Y.

FOLDES, EUGENE, M.D., Adjunct Professor of Gastroenterology, New York Polyclinic Medical School and Hospital, New York, N. Y.

FRADKIN, WILLIAM Z., A.B., M.D., Adjunct Gastroenterologist in Charge of Colitis Clinic, Jewish Hospital of Brooklyn, Brooklyn, N. Y.

GLENN, FRANK, M.D., Professor of Surgery, Cornell University Medical College; Surgeon-in-Chief, New York Hospital, New York, N. Y.

GOVERNALE, SAMUEL L., B.S., M.D., F.A.C.S., Associate in Surgery, Stritch School of Medicine, Loyola University; Chief of Surgery, St. Bernard Hospital, Chicago, Ill.

HARBISON, SAMUEL P., A.B., M.D., Professor of Surgery, University of Pittsburgh; Presbyterian, Allegheny General and Veterans Administration Hospitals, Pittsburgh, Pa.

HARKEN, DWIGHT E., A.B., M.D., Assistant Clinical Professor of Surgery, Harvard Medical School; Surgeon, Peter Bent Brigham Hospital, Boston, Mass.

HARRISON, CHARLES S., Assistant in Surgery, Cornell University Medical College; 1st Assistant Resident Surgeon, New York Hospital, New York, N. Y.

HARVEY, HAROLD D., M.D., Assistant Professor of Clinical Surgery, Columbia University, College of Physicians and Surgeons; Associate Attending Surgeon, Presbyterian Hospital, New York, N. Y.

HENNIG, GEORGE C., M.D., Assistant in Medicine, Columbia University, College of Physicians and Surgeons, New York, N. Y.

KELLER, THEODORE C., M.D., Chief of Laboratory, Mercy Hospital, Miami, Fla.

KENT, EDWARD M., M.D., Associate Professor of Surgery, University of Pittsburgh; Pittsburgh, Pa.

KLEMPERER, PAUL, M.D., Professor of Pathology, Columbia University, College of Physicians and Surgeons; Pathologist, The Mt. Sinai Hospital; Consultant, United States Public Health Service, New York, N. Y.

LICTHMAN, S. S., B.A., M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College; Assistant Physician, New York Hospital; Adjunct Physician, The Mt. Sinai Hospital, New York, N. Y.

LORD, JERE W., JR., A.B., M.D., F.A.C.S., Associate Professor of Clinical Surgery, New York University-Postgraduate Medical School; Attending Surgeon, Bellevue Hospital, 4th Division, New York, N. Y.

LUST, FRANZ J., M.D., New York, N. Y.

MADDEN, JOHN L., M.D., F.A.C.S., Director of Surgery, St. Clare's Hospital, New York, N. Y.

MARSHAK, RICHARD H., M.A., B.S., M.D., Associate Roentgenologist, The Mt. Sinai Hospital, New York, N. Y.

MARTIN, LAY, M.D., F.A.C.P., Assistant Professor of Medicine, The Johns Hopkins University, Baltimore, Md.

MARTIN, W. S., M.D., C.M., M.Eng., Associate, Medical Staff, Sherbrooke Hospital, Sherbrooke, Quebec.

VISIT THE EXHIBITS

MORTON, H. S., M.B., F.R.C.S., F.A.C.S., Assistant Professor of Surgery, McGill University School of Medicine; Associate Surgeon, Royal Victoria Hospital, Montreal, Canada.

MOSENTHAL, HERMAN O., B.A., M.D., Consulting Physician, Bellevue, University, Seaview Hospitals, New York, N. Y.

MOSLEY, JOHN H., M.D., Attending, X-ray Department, Sydenham Hospital, New York, N. Y.

MYERS, PHILIP, M.D., Radiologist, Spring Grove Hospital; Assistant in Roentgenology, Sinai Hospital, Baltimore, Md.

NATHAN, HELMUTH, M., M.D., F.I.C.S., Associate Attending Surgeon, Sydenham Hospital, New York, N. Y.

NEEFE, JOHN R., B.S., M.D., Associate in Medicine, Hospital and School of Medicine, University of Pennsylvania; Member, Commission on Liver Disease, Armed Forces Epidemiological Board, Philadelphia, Pa.

NEWMAN, HERBERT F., B.A., M.D., Associate Clinical Professor of Surgery, New York University-Bellevue Medical Center, New York, N. Y.

PACK, GEORGE T., B.S., M.D., LL.D., Clinical Professor of Surgery, New York Medical College; Associate Professor of Clinical Surgery, Cornell University School of Medicine; Attending Surgeon, Memorial Hospital; Pack Medical Group, New York, N. Y.

PATTERSON, RUSSEL H., A.B., M.D., F.A.C.S., Associate Professor of Clinical Surgery, Cornell University Medical School; Visiting Surgeon, Bellevue Hospital; Director of Surgery, Knickerbocker Hospital, New York, N. Y.

PAULSON, MOSES, M.D., Assistant Professor of Medicine, The Johns Hopkins University; Physician, The Johns Hopkins Hospital and Consultant in Digestive Diseases to its Diagnostic Clinic and Private Out Patient Service, Baltimore, Md.

PAYNE, MARY ANN, B.A., M.A., Ph.D., M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College; Assistant Attending Physician, New York Hospital, New York, N. Y.

POOL, JOHN L., M.D., Assistant Professor of Clinical Surgery, Cornell University School of Medicine; Associate Attending Surgeon, Thoracic Service, Memorial Hospital, New York, N. Y.

PORTER, MILTON R,. A.B., M.D., Associate in Surgery, Columbia University, College of Physicians and Surgeons; Associate Attending Surgeon, Presbyterian Hospital; Assistant Visiting Surgeon, Delafield Hospital, New York, N. Y.

PROPATORIDIS, JORDAN, M.D., Lecturer in Surgery, II University Clinic of Aretaieion Hospital, Athens, Greece.

RICHMAN, ALEXANDER, M.D., Adjunct Physician, Gastroenterology, The Mt. Sinai Hospital, New York, N. Y.

RIESE, JACOB A., B.A., M.D., Chief, Gastrointestinal Clinic, Jersey City Medical Center; Attending Gastroenterologist, North Hudson Hospital, Weehawken, N. J., Jersey City, N. J.

ROUSSELOT. LOUIS M., A.B., M.D., Med. Sci. D., Professor of Clinical Surgery, New York University College of Medicine; Director of Surgery, St. Vincent's Hospital, New York, N. Y.

SCIORSCI, EDWARD F., A.B., M.D., F.I.C.S., F.A.C.S., Chairman, Surgical Committee, St. Francis Hospital; Attending Surgeon, Jersey City Medical Center, Hoboken, N. J.

SELYE, HANS, M.D., Sc.D., Ph.D., F.R.S. (C), Professor and Director of the Institute of Experimental Medicine and Surgery, University of Montreal, Montreal, Canada.

SHAIKEN, JOSEPH, M.D., B.S., M.Sc. (Med.), Associate Professor of Medicine, Marquette University Medical School; Chief, Department of Internal Medicine, Milwaukee County Hospital; Attending Gastroenterologist, Mt. Sinai Hospital, Milwaukee, Wisc.

SHANK, PAUL J., M.D., F.A.C.S., Good Samaritan Hospital; Miami Valley Hospital, Dayton, Ohio.

SHUTKIN, MICHAEL W., B.A., M.D., Assistant Clinical Professor of Medicine, Marquette University; Attending Physician, Mt. Sinai Hospital, Milwaukee County Hospital, St. Luke's Hospital, Milwaukee, Wisc.

SMETANA, HANS F., M.D., Chief, Division of Pathology, Armed Forces Institute of Pathology, Washington, D. C.

VISIT THE EXHIBITS

SNAPPER, I., M.D., Ph.D., Clinical Professor of Medicine, Columbia University, College of Physicians and Surgeons; Physician and Director of Medical Education, The Mt. Sinai Hospital, New York, N. Y.

STAFFORD, ROBERT P., M.D., Good Samaritan Hospital; St. Elizabeth's Hospital, Dayton, Ohio.

STANDARD, SAMUEL, M.D., F.A.C.S., Associate Professor of Clinical Surgery, New York University-Bellevue Medical Center; Visiting Surgeon, Bellevue and University Hospitals; Director of Surgery, Sydenham Hospital, New York, N. Y.

THOMAS J. EARL, B.S., M.S., M.D., Professor of Physiology, The Jefferson Medical College of Philadelphia, Philadelphia, Pa.

TILLINGHAST, A. J., M.D., C.M., X-ray Department, Doctors Hospital, New York, N. Y.

TOCANTINS, LEANDRO M., M.D., Jefferson Medical College and Hospital, Philadelphia, Pa.

UPHAM, ROY, M.D., F.A.C.S., Associate Professor of Medicine and Gastroenterology, New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y.

WANGENSTEEN, OWEN H., B.A., M.D., Ph.D., Professor and Chairman, Department of Surgery, University of Minnesota Medical School, Minneapolis, Minn.

WEINGARTEN, MICHAEL, M.D., Associate Clinical Professor of Medicine, New York University-Postgraduate Medical School; Attending Gastroenterologist, Beth Israel Hospital, New York, N. Y.

WEINTRAUB, SIDNEY, M.D., The New York Hospital, New York, N. Y.

WERTHAM, FREDRIC, M.D., Director, LaFargue Clinic; Director Psychiatric Service, Queens General Hospital, New York, N. Y.

VISIT THE EXHIBITS

SCIENTIFIC SESSIONS

FIRST SESSION

MONDAY MORNING, 20 OCTOBER 1952

WILLIAM W. LERMANN, M.D., President, National Gastroenterological Association, presiding.

9:00 A.M.

SYMPOSIUM ON DISEASES OF THE LIVER:

1. "Hematological Aspects of Hepatic Disease."

Speaker

DR. LEANDRO M. TOCANTINS, Philadelphia, Pa. (By invitation).

9:30 A.M.

2. "Liver Biopsy".

Speaker

DR. JOHN R. NEEFE, Philadelphia, Pa. (By invitation).

10:00 A.M.

3. "The Present Status of Liver Function Tests".

Speaker

DR. S. S. LICHTMAN, New York, N. Y. (By invitation).

10:30 A.M. Recess.

10:45 A.M.

4. "Histopathologic Criteria of Diseases of the Liver".

Speakers

DR. HANS F. SMETANA, Washington, D. C.; DR. THEODORE C. KELLER, Miami, Fla. and MAJOR I. N. DUBIN, M.C., Washington, D. C. (By invitation).

11:15 A.M.

Discussion to be opened by:

DR. JOSEPH POST, New York, N. Y. (By invitation).

VISIT THE EXHIBITS

SECOND SESSION

MONDAY AFTERNOON, 20 OCTOBER 1952

SIGURD W. JOHNSEN, M.D., Vice-President, National Gastroenterological Association, presiding.

2:00 P.M.

5. "Recent Progress in Gastrointestinal Physiology".

Speaker

DR. J. EARL THOMAS, Philadelphia, Pa. (By invitation).

2:30 P.M.

Discussion to be opened by:

DR. FRANKLIN HOLLANDER, New York, N. Y. (By invitation).

2:40 P.M.

6. "Electrogastrography; Its Clinical Aspects".

Speakers

DR. H. S. MORTON, Montreal, Canada and DR. W. S. MARTIN, Montreal, Canada (By invitation).

3:10 P.M.

General Discussion.

3:20 P.M.

7. "Several Problems in Biliary Tract Surgery".

Speaker

DR. HERBERT F. NEWMAN, New York, N. Y. (By invitation).

3:50 P.M.

Discussion to be opened by:

DR. SAMUEL GAINES, New York, N. Y.

4:00 P.M.

ANNUAL MEETING OF THE ASSOCIATION—GENERAL ASSEMBLY

5:00 P.M.

CONVOCATION: Presentation of Certificates.

See special program.

6:30 P.M.

PRESIDENT'S ANNUAL RECEPTION (Admission by card only, obtained at the time of registration).

VISIT THE EXHIBITS

THIRD SESSION

TUESDAY MORNING, 21 OCTOBER 1952

Exhibits will be open from 8:30 A.M. until closing.

LYNN A. FERGUSON, M.D., Vice-President, National Gastroenterological Association, presiding.

9:00 A.M.

SYMPOSIUM FOR THE GENERAL PRACTITIONER:
8. "Acute Lower Abdominal Emergencies".

Speaker

DR. HENRY W. CAVE, New York, N. Y. (By invitation).

9:30 A.M.

9. "Insulin and Diabetes".

Speaker

DR. HERMAN O. MOSENTHAL, New York, N. Y. (By invitation).

10:00 A.M.

10. "Upper Abdominal Pain — Differential Diagnosis".

Speaker

DR. LINN J. BOYD, New York, N. Y. (By invitation).

10:30 A.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

11:00 A.M.

11. "Bleeding from the Gastrointestinal Tract".

Speaker

DR. SAMUEL S. BERGER, Cleveland, Ohio.

11:30 A.M.

12. "Rectal Bleeding".

Speaker

DR. MAX P. COWETT, New York, N. Y. (By invitation).

12:00 Noon

13. "Milestones in the Diagnosis and Treatment of Diarrheal Diseases".

Speaker

DR. WILLIAM Z. FRADKIN, Brooklyn, N. Y.

VISIT THE EXHIBITS

FOURTH SESSION

TUESDAY AFTERNOON, 21 OCTOBER 1952

JAMES T. NIX, M.D., Vice-President, National Gastroenterological Association, presiding.

2:00 P.M.

14. "Present Status of Radiosisotopic Therapy".

Speaker

DR. L. A. ERF, Philadelphia, Pa. (By invitation).

2:30 P.M.

General Discussion.

2:40 P.M.

SYMPOSIUM ON BLEEDING ESOPHAGEAL VARICES AND THE PROBLEM OF PORTAL HYPERTENSION:

Moderator: DR. SAMUEL P. HARBISON, Pittsburgh, Pa.

15. "Portacaval Systemic Shunts".

Speaker

DR. JERE W. LORD, JR. New York, N. Y. (By invitation).

3:00 P.M.

16. "Ligation of the Hepatic and Splenic Arteries in the Treatment of Cirrhosis of the Liver".

Speaker

DR. JOHN L. MADDEN, New York, N. Y. (By invitation).

3:20 P.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

3:50 P.M.

17. "Physiology and Pathology of the Cirrhotic Liver".

Speaker

DR. MARY ANN PAYNE, New York, N. Y. (By invitation).

4:10 P.M.

18. "Mediastinal Packing and Bleeding of Esophageal Varices".

Speaker

DR. EDWARD M. KENT, Pittsburgh, Pa. (By invitation).

7:00 P.M.

ANNUAL BANQUET — HOTEL STATLER, New York, N. Y.

VISIT THE EXHIBITS

FIFTH SESSION

WEDNESDAY MORNING, 22 OCTOBER 1952

ARTHUR A. KIRCHNER, M.D., Vice-President, National Gastroenterological Association, presiding.

9:00 A.M.

19. "The Incidence of the Coexistence of Gastric Ulcer in Esophageal Hiatus Hernia of the Stomach".

Speakers

DR. MAURICE FELDMAN, Baltimore, Md. and DR. PHILIP MYERS, Baltimore, Md. (By invitation).

9:30 A.M.

General Discussion.

9:40 A.M.

20. "Surgical and Medical Treatment of Diaphragmatic Hernia".

Speakers

DR. ROBERT E. FARRAND, Boston, Mass. (By invitation) and DR. DWIGHT E. HARKEN, Boston, Mass.

10:10 A.M.

General Discussion.

10:20 A.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

10:50 A.M.

21. "The General Adaptation Syndrome and Gastroenterology".

Speaker

DR. HANS SELYE, Montreal, Canada (By invitation).

11:20 A.M.

Discussion to be opened by:

DR. FLANDERS DUNBAR, New York, N. Y. (By invitation).

11:40 A.M.

22. "The Clinical Oneness of Nonspecific Intestinal Inflammatory States".

Speaker

DR. MOSES PAULSON, Baltimore, Md. (By invitation).

12:10 P.M.

Discussion to be opened by:

DR. ASHER WINKELSTEIN, New York, N. Y. (By invitation).

VISIT THE EXHIBITS

SIXTH SESSION

WEDNESDAY AFTERNOON, 22 OCTOBER 1952

ROY UPHAM, M.D., Secretary-General, National Gastroenterological Association, presiding.

2:00 P.M.

PANEL DISCUSSION ON GASTROINTESTINAL X-RAY METHODS, DIAGNOSIS AND TREATMENT:

Moderator: DR. WILLIAM W. LERMANN, Pittsburgh, Pa.
Participants: DR. LAY MARTIN, Baltimore, Md. (By invitation).
DR. FREDERIC W. BANCROFT, New York, N. Y.
DR. SIDNEY WEINTRAUB, New York, N. Y. (By invitation).

SEVENTH SESSION

WEDNESDAY EVENING, 22 OCTOBER 1952

ANTHONY BASSLER, M.D., Honorary President. National Gastroenterological Association, presiding.

8:00 P.M.

23. "Significant Factors in the Etiology of Gastrojejunal Ulcer".

Speaker

DR. MICHAEL W. SHUTKIN, Milwaukee, Wisc.

8:15 P.M.

24. "The Diagnosis and Treatment of Intractable Peptic Ulcer".

Speaker

DR. JOSEPH SHAIKEN, Milwaukee, Wisc.

8:30 P.M.

25. "Rupture of Echinococcus Cyst of the Liver into the Bile Ducts".

Speaker

DR. JORDAN PROPATORIDIS, Athens, Greece.

8:45 P.M.

26. "Some Interesting Experiences with Jaundice".

Speaker

DR. JACOB A. RIESE, Jersey City, N. J.

9:00 P.M.

27. "Antiretentional Migraine Therapy".

Speaker

DR. EUGENE FOLDES, New York, N. Y.

VISIT THE EXHIBITS

9:15 P.M.

28. "The Relationship of the Esophagus to Heartburn".

Speaker

DR. EDWIN BOROS, New York, N. Y.

9:30 P.M.

29. "Complete Situs Viscerus Inversus Associated with Cholelithiasis and Complicated by Carcinoma of the Gallbladder".

Speakers

DR. PAUL J. SHANK, Dayton, Ohio and DR. ROBERT P. STAFFORD, Dayton, Ohio (By Invitation).

9:45 P.M.

30. "Endometrioma of the Colon and Its Treatment".

Speakers

DR. SAMUEL L. GOVERNALE, Chicago, Ill. and DR. CARLO FIORETTI, Chicago, Ill. (By invitation).

10:00 P.M.

31. "Postoperative Abdominal Distention".

Speaker

DR. EDWARD F. SCIORSCI, Hoboken, N. J.

VISIT THE EXHIBITS

COURSE IN POSTGRADUATE GASTROENTEROLOGY

SURGICAL COORDINATOR AND CO-CHAIRMAN
OWEN H. WANGENSTEEN, B.A., M.D., Ph.D., Minneapolis, Minn.

MEDICAL COORDINATOR AND CO-CHAIRMAN
I. SNAPPER, M.D., Ph.D., New York, N. Y.

FIRST SESSION

THURSDAY MORNING, 23 OCTOBER 1952

FELIX CUNHA, M.D., President, National Gastroenterological Association, presiding.

9:00 A.M.
Address of Welcome—
DR. FELIX CUNHA.

9:15 A.M.
1. "Lesions of the Oral Region".

Speaker
DR. ADOLPH BERGER, New York, N. Y.

9:45 A.M.
2. "Roentgen Diagnosis in Esophageal Diseases".

Speaker
DR. ARTHUR J. BENDICK, New York, N. Y.

10:15 A.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

10:45 A.M.
3. "Esophageal Cancer: Diagnostic and Therapeutic Problems".

Speaker
DR. JOHN L. POOL, New York, N. Y.

VISIT THE EXHIBITS

11:15 A.M.

4. "Subject to be announced".

Speaker

DR. OWEN H. WANGENSTEEN, Minneapolis, Minn.

SECOND SESSION

THURSDAY AFTERNOON, 23 OCTOBER 1952

2:00 P.M.

5. "Diseases of the Stomach and Duodenum".

Speaker

DR. SOL FINEMAN, New York, N. Y.

2:30 P.M.

6. "Modern Trends in Gastroscopy".

Speaker

DR. HARRY BAROWSKY, New York, N. Y.

3:00 P.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

3:30 P.M.

7. "Current Status of Medical Management of Peptic Ulcer".

Speakers

DR. CHARLES A. FLOOD, New York, N. Y. and DR. GEORGE C. HENNIG, New York, N. Y.

4:00 P.M.

8. "Gastric Carcinoma".

Speaker

DR. HAROLD D. HARVEY, New York, N. Y.

VISIT THE EXHIBITS

4:30 P.M.

9. "Problems in Gastric Surgery".

Speakers

Dr. Russel H. Patterson, New York, N. Y. and Dr. Jose M. Cantellops, New York, N. Y.

THIRD SESSION

FRIDAY MORNING, 24 OCTOBER 1952

9:00 A.M.

10. "Internal Herniae — Pathology, Clinic, X-ray, Therapy".

Speakers

Dr. Helmuth Nathan, New York, N. Y. and Dr. John H. Mosley, New York, N. Y.

9:30 A.M.

11. "The Gastric Cancer Problem".

Speaker

Dr. William A. Cooper, New York, N. Y.

10:00 A.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

10:30 A.M.

12. "Postcholecystectomy Syndrome".

Speaker

Dr. Roy Upham, New York, N. Y.

11:00 A.M.

13. "X-ray of the Colon".

Speaker

Dr. Franz J. Lust, New York, N. Y.

VISIT THE EXHIBITS

11:30 A.M.

14. "Clinical Manifestations of Chronic Amebiasis".

Speaker

DR. MICHAEL WEINGARTEN, New York, N. Y.

12:00 Noon

BUFFET LUNCHEON (Admission by card only)

FOURTH SESSION

FRIDAY AFTERNOON, 24 OCTOBER 1952

2:00 P.M.

15. "The Diagnosis of Pancreatic Disease".

Speaker

DR. ALEXANDER RICHMAN, New York, N. Y.

2:30 P.M. Recess to visit the Commercial, Technical and Scientific Exhibits.

3:00 P.M.

16. "Pancreatic Cancer — An Evaluation of Total Pancreatectomy".

Speaker

DR. MILTON R. PORTER, New York, N. Y.

3:30 P.M.

17. "Surgical Indications and Type of Surgical Therapy in Various Splenopathies".

Speaker

DR. LOUIS M. ROUSSELOT, New York, N. Y.

4:00 P.M.

18. "Surgical Aspects of Diverticulitis".

Speakers

DR. FRANK GLENN, New York, N. Y. and DR. CHARLES S. HARRISON, New York, N. Y.

4:30 P.M.

19. "Psychotherapy in Disorders of the Gastrointestinal Tract".

Speaker

DR. FREDERIC WERTHAM, New York, N. Y.

VISIT THE EXHIBITS

FIFTH SESSION

SATURDAY MORNING, 25 OCTOBER 1952

This entire session will be held at The Mt. Sinai Hospital, 100th Street and Fifth Avenue.

9:30 A.M.
Clinical Pathological Conference
DR. PAUL KLEMPERER, New York, N. Y.

10:30 A.M.
20. "Roentgen Aspects of Diseases of the Small Intestine".
Speaker
DR. RICHARD H. MARSHAK, New York, N. Y.

11:00 A.M.
21. "Diseases of the Small Intestine".
Speaker
DR. DAVID ADLERSBERG, New York, N. Y.

SIXTH SESSION

SATURDAY AFTERNOON, 25 OCTOBER 1952

This session will again be held at the Hotel Statler.

2:00 P.M.
22. "X-ray Diagnosis in Biliary Tract Disorders".
Speaker
DR. A. J. TILLINGHAST, New York, N. Y.

2:30 P.M.
23. "Surgery of the Gallbladder".
Speaker
DR. SAMUEL STANDARD, New York, N. Y.

VISIT THE EXHIBITS

3:00 P.M.

24. "Surgery of the Colon".

Speaker

DR. GEORGE T. PACK, New York, N. Y.

3:30 P.M.

25. "Surgery in Proctological Cases".

Speaker

DR. R. J. CONNORS, Fall River, Mass.

VISIT THE EXHIBITS

SCIENTIFIC EXHIBITS

The Scientific Exhibits will be in the Exhibit Hall and will be open at the following times:

TUESDAY, 21 October 1952–8:30 A.M. to 5:30 P.M.

WEDNESDAY, 22 October 1952 – 9:00 A.M. to 5:30 P.M.; 8:00 P.M. to 11:00 P.M.

THURSDAY, 23 October 1952–9:00 A.M. to 5:30 P.M.

FRIDAY, 24 October 1952–9:00 A.M. to 3:00 P.M.

BOOTH S-1 **"A New Polyethylene Gastroduodenal Tube".**
DRS. M. J. MATZNER and H. ZAROVITZ, Brooklyn, N. Y.

BOOTH S-2 **"Perianal Tuberculous Infection".**
DR. JULIUS GERENDASY, Jersey City, N. J.

BOOTH S-3 **"An Anorectoplasty for Complicated and Extensive Hemorrhoids".**
DR. EMIL GRANET, New York, N. Y.

BOOTH S-4 **"Gallbladder Disease".**
DR. BRUCE C. LOCKWOOD, Detroit, Mich.

BOOTH S-5 **"The Effect of Prantal Upon Gastric Motility and Secretion in the Human".**
DRS. LOUIS E. ZIMMER, DANIEL BURBANK, JOHN CONIARIS and RALPH MAFFEY, Newark, N. J.

BOOTH S-6 **"The Electrogastrograph".**
DRS. H. S. MORTON and W. S. MARTIN, Montreal, Canada

BOOTH S-7 **"A Technic for the Control of Anorectal Pain".**
DR. J. M. GROSS, BROOKLYN, N. Y.

BOOTH S-8 **"Surgical Anatomy of the Male Anal Perineum".**
DR. EDWARD LEVY, Bronx, N. Y.

BOOTH S-9 **"Diarrheal Diseases in Gastroenterology—A New Approach".**
DR. WILLIAM Z. FRADKIN, Brooklyn, N. Y.

BOOTH S-10 **"How to Reduce Mortality from Intestinal Obstruction".**
DR. GUSTAV ZECHEL, Chicago, Ill.

VISIT THE EXHIBITS

TECHNICAL EXHIBITORS

(Those attending the Convention sessions are urged to take advantage of the time in between the presentation of papers and sessions, to visit the technical exhibits and become acquainted with many new products and new equipment on display)

AMES COMPANY, INC., Elkhart, Ind. (Booth 7), will review chemical oxidation products derived from bile acids. Effect of these acids on hepatic blood flow, cholesterol metabolism and on volume output and composition will be charted for discussion.

J. BEEBER COMPANY, INC., New York, N. Y. (Booth 4), is pleased to present the newest diagnostic equipment, as well as that for treatment of diseases: The latest Mattern X-Ray Units, which makes diagnosis easier for the Gastroenterologist; the Raytheon Microwave Diathermy, which is considered one of the foremost advances in Physical Medicine; and the Beck Lee Direct Writing Electrocardiograph.

BURTON, PARSONS & COMPANY, Washington, D. C. (Booth 5), will feature Konsyl and L.A. Formula, the original refined psyllium bulk laxatives. L.A. Formula has been shown through clinical trial to be as much as 8 times more effective than methylcellulose in the treatment of severe chronic constipation. Konsyl is the all-purpose bulk laxative which contains 100 per cent bulk without the addition of sugars or other deleterious substances. It provides maximum bulk action per minimum dose.

CAMERON SURGICAL SPECIALTY COMPANY, Chicago, Ill. (Booth 21), will display the Omniangle Gastroscope – the generally accepted standard throughout the world. No other gastroscope approaches the efficiency of a Cameron Omniangle Gastroscope. Other items are the Crump Ductlite, Esophageal Stylet, Boros Flexible Esophagoscope, Broncho-Esophago-Laryngoscopic scopes, and a large assortment of stainless steel and Surgimold distally and proximally lighted Rectal Endoscopes.

THE COCA-COLA COMPANY, Atlanta, Ga. (Lounge), will serve ice-cold Coca-Cola through the courtesy and cooperation of the Coca-Cola Company.

EDER INSTRUMENT COMPANY, Chicago, Ill. (Booth 14), will exhibit their Gastroscopic Instruments, the standard flexible, the adjustable tip and the new suction biopsy Gastroscope. The Eder-Hufford flexible Esophagoscope with two optical examining telescopes should be of interest to the profession. The new improved proctoscopic table convertible into a standard examining table is also one of the latest developments along with rectal and other diagnostic instruments.

GRUNE & STRATTON, INC., New York, N. Y. (Booth 3). Two new titles are of exceptional interest: Iason's *Gastric Cancer* and Goldman's *Fundamentals of Clinical Cancer.* Of continued interest are Crohn's *Regional Ileitis,* Schindler's *Gastritis,* Fradkin's *Diarrheal Diseases,* the new journal, *Metabolism,* and, particularly for Diagnosis, Bauer's *Differential Diagnosis of Internal Diseases* and Storch's *Fundamentals of Clinical Fluoroscopy.* Fields related to Gastroenterology are fully represented.

THE HARROWER LABORATORY, INC., Jersey City, N. J. (Booth 13), will present Prulose Complex Liquid – a new product containing a new laxative, diacetylhydroxy-phenylisatin, the recently isolated active principle of California prunes. Pharmacological and clinical data are featured.

Reprints, samples, and literature will be availale at the exhibit.

IVES-CAMERON COMPANY, INC., New York, N. Y. (Booth 8), cordially invites you to stop at their booth where trained representatives will be happy to discuss the use of surface active agents and nutritional supplements in gastrointestinal diseases.

J. B. LIPPINCOTT COMPANY, Philadelphia, Pa. (Booth 10), will present for your approval, a display of professional books and journals geared to the latest and most important trends in current medicine and surgery. These publications, written and edited by men active in clinical fields and teachings, are a continuation of more than 100 years of traditionally significant publishing.

VISIT THE EXHIBITS

THE MALLON CHEMICAL CORPORATION, New York, N. Y. (Booth 12), subsidiaries of the Doho Chemical Corporation, makers of *Auralgan, Otosmosan,* and *Rhinalgan,* are pleased to exhibit *Rectalgan,* the liquid topical anesthesia for the immediate symptomatic relief of pain and discomfiture in hemmorhoids, pruritus and perineal pain following suturing, also many other uses pre- and postoperatively.

THE NATIONAL DRUG COMPANY, Philadelphia, Pa. (Booth 20), pioneer in the clinical application of resin therapy, will feature Resion, an intestinal absorbent; Resinat H-M-B, a polyamine exchange resin with homatropine methylbromide, for the treatment of peptic ulcer; and Natrinil, a cation exchange resin for the control of edema. Trained representatives will be in attendance to discuss our resin preparations and other specialties.

WILLIAM H. RORER, INC., Philadelphia, Pa. (Booth 2), will display Suspension Maalox, a new antacid suspension composed of special colloidal grades of Magnesium Hydroxide and Aluminum Hydroxide. Maalox was originated to provide the patient with all the advantages of Aluminum Hydroxide Gel USP but to eliminate the constipation often caused by that drug, and to improve its taste. It has been subjected to intense clinical testing and found advantageous, particularly for peptic and gastric ulcer and for heartburn due to gastritis.

SANDOZ PHARMACEUTICALS, New York, N. Y. (Booth 1), invite you with a great deal of pride to visit their Scientific Exhibit. Their New York representatives will glady welcome you.

SCHENLEY LABORATORIES, INC., Lawrenceburg, Ind. (Booth 17). For useful information on their progressive line, visit their exhibit. Titralac, Schenley's unique antacid is now available in liquid as well as in tablet and powder form. Sedamyl is also featured. Providing sedation without hypnosis, Sedamyl is ideal for daytime use to relieve anxiety common to today's harried life.

SCHERING CORPORATION, Bloomfield, N. J. (Booth 9). Members of the National Gastroenterological Association and their guests are cordially invited to visit the Schering exhibit where new therapeutic developments will be featured.

Schering representatives will be present to welcome you and to discuss with you these products of their manufacture.

G. D. SEARLE & CO., Chicago, Ill. (Booth 11). You are cordially invited to visit their booth where their representatives will be happy to answer any questions regarding Searle Products of Research.

Featured will be Banthine, the true anticholinergic drug for the treatment of peptic ulcers; Dramamine, for the prevention and active treatment of motion sickness; and Alidase, Searle brand of hyaluronidase which permits subcutaneous feeding at intravenous speed.

Other time proven products of Searle Research on which information may be obtained are Searle Aminophyllin in all dosage forms, Metamucil, Ketochol, Floraquin, Kiophyllin, Diodoquin, Pavatrine, and Pavatrine with Phenobarbital.

E. R. SQUIBB & SONS, New York, N. Y. (Booth 6), will feature new Squibb products and new brochures of useful interest to you on products already introduced. As in former years, your Squibb representative again cordially invites you to visit the Squibb booth.

FREDERICK TROUT COMPANY, INC., Atlanta, Ga. (Booth 18), will feature *Vermantin* for hypertension. The formula contains two hypotensive agents plus a mild sedative and capillary protectant. *Combichole* a combination of chemically pure bile acids for hydrocholeresis plus fat digestion. *Calsamate* a buffered analgesic to prevent a gastric upset, fortified with Vitamin C.

WINTHROP STEARNS, Inc., New York, N. Y. (Booth 13), extends a cordial invitation to visit its booth, where representatives will be on hand to serve you. Featured will be *Telepaque,* for superior oral cholecystography; *Mucilose Compound Tablets,* the new physiologic bulk laxative; *Diodrast 35%,* for operative and postoperative cholangiography; *Essenamin Compound,* pleasant tasting protein concentrate; *Trimucolan,* triple mucin-antacid.

VISIT THE EXHIBITS

Election of officers, under the provisions of the Constitution and By-laws, will take place at this time.

Convocation Ceremony

The Convocation Ceremony, at which certificates of affiliation will be presented in person to newly elected Members, Associate Fellows, Fellows, and those advanced in the various categories during the year, will follow the Annual Meeting of the Association at 5:00 P.M. on Monday afternoon, 20 October 1952, at the Hotel Statler in New York, N. Y.

This year again, those participating in the Convocation Ceremony will wear academic costume, and an interesting program has been planned.

Members, their families, guests and friends are invited to attend.

President's Annual Reception

The President's Annual Reception, again sponsored by Winthrop-Stearns, Inc., will be held immediately following the Convocation Ceremony on Monday evening, 20 October 1952, at 6:30 P.M. Members of the Association, their friends, guests, as well as those present with the technical exhibits are cordially invited to attend. Admission cards may be secured at the time of registration at the registration desk.

Scientific Exhibits

This year again we will have a scientific exhibit as part of the scientific program.

A great many interesting presentations have been prepared and will be on display in a separate section from Tuesday through Friday of the Convention week.

Annual Banquet

The Annual Banquet of the National Gastroenterological Association will be held at the Hotel Statler in New York, N. Y., on Tuesday evening, 21 October 1952, at 7:00 P.M. to be preceded by cocktails.

Course in Postgraduate Gastroenterology

Immediately following our Seventeenth Annual Convention, the National Gastroenterological Association is conducting a Course in Postgraduate Gastroenterology on 23, 24, 25 October 1952, at the Hotel Statler in New York, N. Y.

A distinguished faculty, chosen from the medical schools in and around the New York area, headed by Dr. Owen H. Wangensteen, Professor and Chair-

man of Department of Surgery, University of Minnesota Medical School, Co-chairman and Surgical Co-ordinator, and Dr. I. Snapper, Director of Medical Education of The Mt. Sinai Hospital, New York City, Co-Chairman and Medical Co-ordinator will present the Course.

Admission to the Course will be limited to those who hold matriculation cards indicating that they have paid the fee for the Course.

Nominating Committe Report

The nominating committee of the National Gastroenterological Association, consisting of Dr. William W. Lermann, Pittsburgh, Pa., chairman; Dr. Felix Cunha, San Francisco, Calif.; Dr. G. Randolph Manning, New York, N. Y. and Dr. E. A. Marshall, Cleveland, Ohio, has submitted the following slate of candidates to be voted upon at the annual meeting of the National Gastroenterological Association in October.

Officers

President-Elect.....Sigurd W. Johnsen, M.D., Passaic, N. J.
1st Vice-President.....Lynn A. Ferguson, M.D., Grand Rapids, Mich.
2nd Vice-President.....James T. Nix, M.D., New Orleans, La.
3rd Vice-President.....Arthur A. Kirchner, M.D., Los Angeles, Cal.
4th Vice-President.....C. Wilmer Wirts, M.D., Philadelphia, Pa.
Secretary-General.....Roy Upham, M.D., New York, N. Y.
Secretary.....A. X. Rossien, M.D., Kew Gardens, N. Y.
Treasurer.....Elihu Katz, M.D., New York, N. Y.

For Members of the National Council

For 4 years:

Frank J. Borrelli, M.D., Tuckahoe, N. Y.
H. Necheles, M.D., Chicago, Ill.
Louis L. Perkel, M.D., Jersey City, N. J.
C. J. Tidmarsh, M.D., Montreal, Canada
Fred H. Voss, M.D., Phoenicia, N. Y.

In Memoriam

We record with profound sorrow the passing of Dr. Thomas H. Cuddy, Fellow, of Winnipeg, Manitoba.

We extend our deepest sympathies to the members of the bereaved family.

BOOK REVIEWS

TOBACCO AND THE CARDIOVASCULAR SYSTEM: Grace M. Roth, Ph.D., Associate Professor of Experimental Medicine, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota and Consultant in Section on Physiology, Mayo Clinic, Rochester, Minnesota. 66 pages. Charles C. Thomas, Springfield, Ill. Price

This little interesting monograph on "The Effects of Smoking and of Nicotine on Normal Persons" should be welcomed by all those who are interested in the physiologic aspects of smoking on the cardiovascular system of men in good health. Dr. Roth finds on the basis of scientific and experimental investigations, that the smoking of tobacco is most likely a contributing factor and not a primarily etiologic one in the production of cardiovascular disease. In normal individuals, smoking (tobacco) usually causes a rise in blood pressure and pulse rate with simultaneous constriction of the peripheral blood vessels of the extremities. Nicotine produces the vascular effects in the smoke. More effects are noted when smoke is inhaled and the tobacco is moist. Drinking cocktails will not necessarily nullify the effect of smoking.

LES SYNDROMES DOULOUREUX DE LA REGION EPIGASTRIQUE: Rene A. Guttman, et al. Fifth edition, 2 vols., paper covers; pages 820; 859 with 689 illustrations. Gaston Doin & Cie, Paris, 1951-1952.

This two volume text by Guttman, Roger and Porak has reached the fifth edition. Discussions and numerous illustrations describe clinical forms of epigastric pain, ulcer and other gastrointestinal ailments.

Liver diseases, avitaminosis and their effect on digestive tract diseases are clearly presented.

The therapy outlined by the authors may be puzzling as it differs with those employed in the United States. However, to physicians who are conversant with the French language, the contents of the two volumes will aid them to better understand and treat the painful syndromes of the epigastric region.

DER DARMVERSCHLUSS UND SONSTIGE WEGSTORUMGEN DES DARMES: Professor Dr. R. Stich, Gottingen. Pages 188, illustrated, Walter de Gruyter, Berlin. 1952, price DM., 16.80.

In this well written and illustrated book the author wishes to convey to the reader the nature, diagnosis and treatment of intestinal obstruction.

The literature dealing with this subject is well represented, an unusual procedure in books written abroad. There is also a comprehensive index.

The reviewer suggests that the publishers would find it to their advantage to have this little volume translated into other languages.

★ ★

First Lieutenant Henry A. Commiskey, USMC Medal of Honor

ONE SEPTEMBER DAY, near Yongdungp'o, Korea, Lieutenant Commiskey's platoon was assaulting a vital position called Hill 85. Suddenly it hit a field of fire from a Red machine gun. The important attack stopped cold. Alone, *and armed with only a .45 calibre pistol,* Lieutenant Commiskey jumped to his feet, rushed the gun. He dispatched its five-man crew, then reloaded, and cleaned out another foxhole. Inspired by his daring, his platoon cleared and captured the hill. Lieutenant Commiskey says:

"After all, only a limited number of Americans need serve in uniform. But, thank God there are millions *more* who are proving their devotion in another vitally important way. *People like you,* whose *50-billion-dollar investment* in U.S. Defense Bonds helps make America so strong no Commie can crack us from within! *That counts plenty!*

"Our bullets alone can't keep you and your family peacefully secure. But our bullets—*and your Bonds*—do!"

★ ★ ★

Now E Bonds earn more! 1) All Series E Bonds bought after May 1, 1952 average 3% interest, compounded semiannually! Interest now starts after 6 months and is higher in the early years. 2) *All maturing E Bonds* automatically go on earning *after maturity*—and at the new higher interest! Today, start investing in better-paying Series E Bonds through the Payroll Savings Plan where you work! Or inquire at any Federal Reserve Bank or Branch about the Treasury's brand-new bonds, Series H, J, and K.

Peace is for the strong! For peace and prosperity save with U.S. Defense Bonds!

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VISIT THE EXHIBITS

"...the universal disease of our times"[1]

anxiety

responds to

Gentle

SEDAMYL

[ACETYLBROMDIETHYL ACETYLCARBAMIDE SCHENLEY]

Trademark

ideal for daytime use

When patients need a cushion against the anxieties of the day, SEDAMYL® provides gentle, low-level sedation, without recourse to barbiturates.

SEDAMYL quickly overcomes anxiety and nervousness without causing drowsiness or impairing perception. Under its subtle yet distinct influence, the patient simply feels he is having one of his "good" days . . . and is thus enabled to carry on his usual activities with poise and efficiency.

1. Ebaugh, F. G.: Postgrad. Med. 4: 208, 1948.

SUPPLIED:
Tablets containing 0.26 Gm. (4 gr.), in tubes of 20's, bottles of 100's and 1000's

Professional literature and samples are available on your request

SCHENLEY LABORATORIES, INC.
LAWRENCEBURG, INDIANA

schenley

First Lieutenant Carl H. Dodd Medal of Honor

"USE MARCHING FIRE—and *follow me!*" Shouting this command, Lieutenant Carl Dodd struck out in advance of his platoon to lead the assault on Hill 256, near Subuk, Korea. During the fierce in-fighting that followed, he constantly inspired his men by his personal disregard of death. Once, alone, he wiped out a machine gun nest; another time, a mortar. After two furious days, Dodd's outnumbered, but spirited, force had won the vital hill.

"You were helping, too," says Lieutenant Dodd. "You and the millions of other citizens who have bought Defense Bonds. For your Bonds, *which keep America strong*, were behind the productive power that gave us the weapons we used.

"I hope you'll go on buying Bonds—always. Because your Bonds—and our bayonets—make an unbeatable combination for keeping safe the land that we all love!"

* * *

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Peace is for the strong! For peace and prosperity save with U.S. Defense Bonds!

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a dual approach
to better carbohydrate
metabolism

TAKA-COMBEX®

When the nutritional status is threatened, **TAKA-COMBEX** provides a dual action which assures adequate vitamin intake as well as proper absorption and utilization of carbohydrates. **TAKA-COMBEX** supplies important factors of the B complex plus Taka-Diastase,® one of the most potent starch digestants known. In addition the Kapseals also contain vitamin C.

In pregnancy, during illness and convalescence, and in the management of geriatric patients, this enzyme-vitamin combination is a most valuable dietary adjunct: the vitamins assist carbohydrate metabolism, while the enzyme not only facilitates starch digestion but also enhances absorption of vitamin B.

KAPSEALS® TAKA-COMBEX

Each Kapseal contains:

Taka-Diastase (Aspergillus Oryzae Enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	10 mg.
Vitamin B_2 (Riboflavin)	10 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Vitamin B_{12} (Cyanocobalamin)	1 mcg.
Pantothenic Acid (As the Sodium Salt)	3 mg.
Nicotinamide (Niacinamide)	10 mg.
Vitamin C (Ascorbic Acid)	30 mg.
Liver Concentrate N.F.	0.17 Gm.
Liver Fraction No. 2 N.F.	0.17 Gm.

In bottles of 100 and 1000.

ELIXIR TAKA-COMBEX

Each teaspoonful (4 cc.) contains:

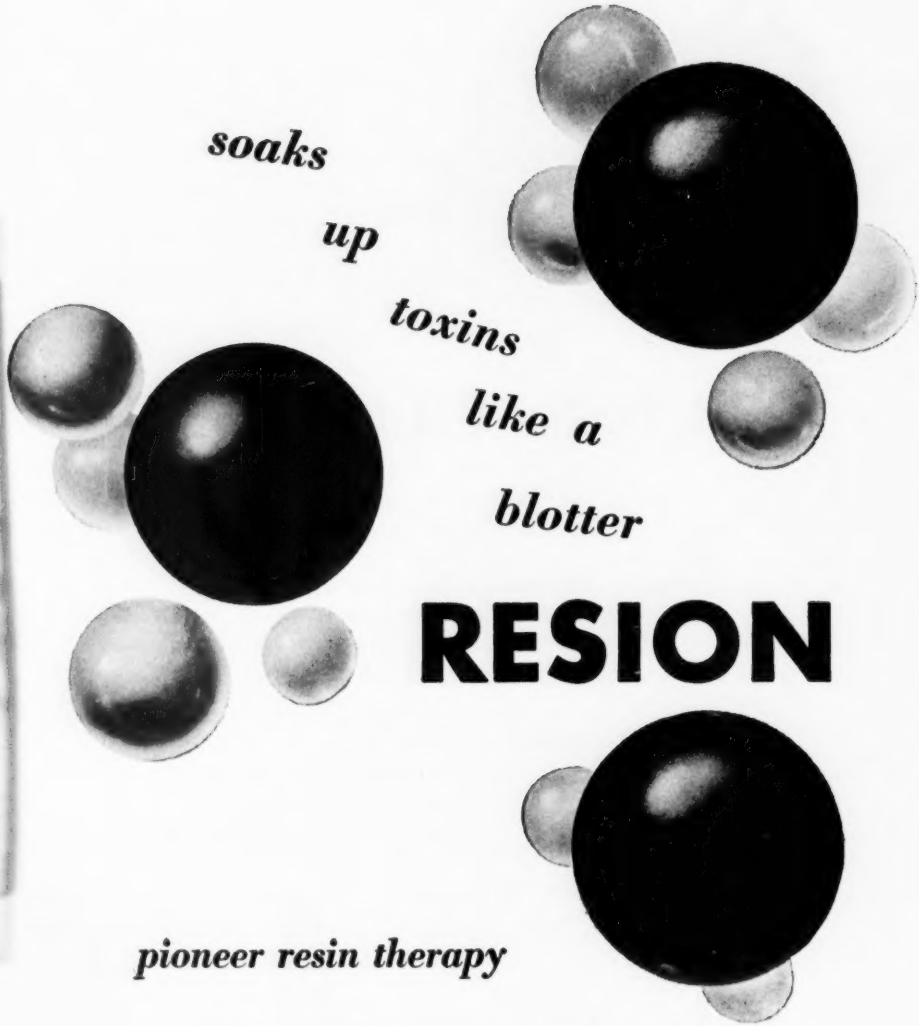
Taka-Diastase (Aspergillus Oryzae Enzymes)	2½ gr.
Vitamin B_1 (Thiamine Hydrochloride)	2 mg.
Vitamin B_2 (Riboflavin)	1 mg.
Vitamin B_6 (Pyridoxine Hydrochloride)	0.5 mg.
Pantothenic Acid (As the Sodium Salt)	2 mg.
Nicotinamide (Niacinamide)	5 mg.

In 16-ounce bottles.

MEDICAMENTA VERA

Parke, Davis + Company

DETROIT, MICHIGAN



RESION

pioneer resin therapy

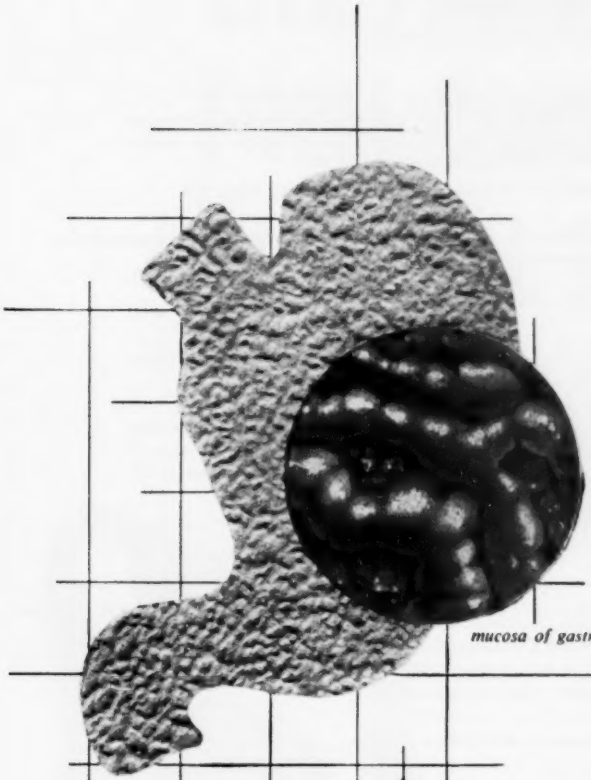
RESINAT—the ANION exchange resin. Inhibits pepsin. Normalizes hydrochloric acid. Adsorbs acid in the stomach, releases it harmlessly in the alkaline small intestine. Indicated in PEPTIC ULCER.

NATRINIL—the CATION exchange resin. For sodium withdrawal. Indicated in CONGESTIVE HEART FAILURE, EDEMATOUS STATES, HYPERTENSION.

SEE OUR EXHIBIT AT BOOTH 20

for

gastritis



mucosa of gastritis

maalox®

Suspension Maalox-Rorer is a colloidal suspension of the *hydroxides* of Magnesium and Aluminum. It is pleasant to taste. Continuous clinical use has demonstrated that it causes a *quick satisfactory relief* of pain and discomfort caused by gastritis.

The dose is two to four fluidrachms.

supplied: In 355 cc. (12 fluidounce) bottles. Also in tablets (Each Maalox tablet is equivalent to one fluidrachm of Suspension). *Samples will be sent promptly on request.*

WILLIAM H. RORER, INC.

Drexel Bldg., Independence Square

Philadelphia 6, Penna.

SEE OUR EXHIBIT AT BOOTH 2

"Let's get down to cases"

"Although in experimental ulcers both the acid factor and the mucosal resistance factor are concerned, we have examples in which the acid factor predominates and others in which a decrease in the defensive properties of the mucosa predominates."*

*Peptic Ulcer. A. C. Ivy, M. I. Grossman and W. H. Bachrach, Blakiston Publishing Co., Phila., 1950.

Comprehensive therapy—whole duodenal substance, VIODENUM—provides an effective natural antacid plus factors which stimulate the mechanisms of repair and defense.

"Viodenum . . . increased the total volume of gastric secretion . . ." yet "Viodenum decreased the free acid . . ."*

*S. Krasnow, F. Steigmann and L. L. Hardt, Comparison of Effectiveness of Various Antacids on Gastric Acidity. Am. J. Dig. Dis., 17:242 (1950).

peptic ulcer

Dr. P. J. Raimondi treated 59 proven cases of duodenal ulcer with Viodenum. He states, "A decrease in the annual rate of recurrence of symptoms was observed in patients with the highest frequency of exacerbations prior to treatment."*

*P. J. Raimondi, Treatment of Duodenal Ulcers with Desiccated, Defatted Duodenal Powder. Permanente Foundation Med. Bull., 8:4 (October), 1950.

Dr. Garnett Cheney treated 30 cases of ulcerative colitis. He states that Viodenum offers ". . . great promise in effecting a complete remission and possibly even a clinical cure . . . whole duodenal substance or Viodenum apparently promotes healing of the bowel by supplying some anti-ulcer factor . . ."*

*Medical Management of Gastrointestinal Disorders. Garnett Cheney, Yearbook Publishers, 1950.

ulcerative colitis

"Duodenal substance (Viodenum) was administered to 35 patients . . . the results obtained in 85% of the patients were very favorable . . . Viodenum may be considered a very valuable aid in the therapy of chronic ulcerative colitis."*

*M. H. Streicher, J. Lab. Clin. Med. 33, 1633 (1948).

Viodenum, *the comprehensive approach:*

1. **Provides an effective natural antacid.**
2. **Provides factors which stimulate the mechanisms of repair and defense.**
3. **Provides natural mucin to soothe and protect irritated mucosa.**
4. **Stimulates gastric secretion yet decreases the free acid.**

Whole duodenal substance desiccated and defatted at body temperature.
Available in powder or ten grain tablets.

Literature available upon request

Viodenum

VIOBIN CORPORATION
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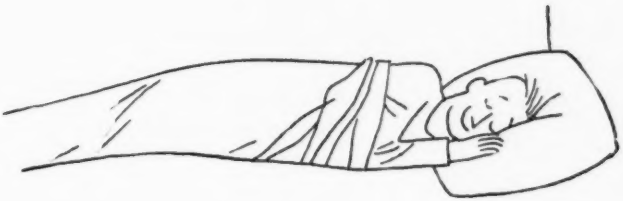
GIVE PROMPT RELIEF FROM CONSTIPATION WITH SAL HEPATICA®



Patients want prompt relief from constipation. Provide it with antacid SAL HEPATICA. There is no laxative lag when SAL HEPATICA is used.

RESTFUL SLEEP is not impaired when laxation occurs before bedtime. Assure this by recommending that SAL HEPATICA be taken one-half hour before dinner.

ACTIVE DAYS, free from the discomforts of constipation, are possible if SAL HEPATICA is taken one-half hour before breakfast. Laxation usually occurs within the hour.

THE GASTRIC HYPERACIDITY which frequently is concomitant with constipation is relieved by this antacid saline laxative.

GENTLE ACTION, freedom from abdominal griping, may be obtained by regulation of dosage.

EFFERVESCENT, PLEASANT-TASTING, SAL HEPATICA is acceptable to patients.

BRISTOL-MYERS COMPANY, 19 WEST 50 STREET, NEW YORK 20, N. Y.

VISIT THE EXHIBITS

l.a.formula

". . . proved considerably more effective than methylcellulose as a bulk laxative, and (was) also superior to previous laxatives such as milk of magnesia, mineral oil, cascara or a phenolphthalein preparation."[1]

l.a.formula

As much as 8 times more effective than Methylcellulose

In a study[1] comparing the effectiveness of psyllium therapy with methylcellulose and selected irritant cathartics, the psyllium preparation, L.A. Formula, brought prompt improvement to 77.5 per cent (18 cases) of 23 patients, many with extreme bowel difficulties.

Conversely, this same group when placed on methylcellulose showed improvement in *only* 9 per cent (2 cases) of the 23 patients. Moreover, when as many as 15 methylcellulose tablets daily met with only partial success, "The large dose was objected to and refused."

In this same study, which included a total of 101 cases limited largely to a notoriously refractive group, Cass and Wolf concluded that, "In severe types of constipation from 73 to 82 per cent of patients were improved on psyllium therapy."

Berberian, et al,[2] have also reported that the addition of 1 part psyllium to 4 parts methylcellulose produced " . . . up to 87 per cent more moisture-retaining and bulk-forming power than the simple methylcellulose tablet of the same weight." This same addition of psyllium to methylcellulose produced ". . . increased bulk of stool immediately from the first day of medication, whereas plain methylcellulose caused a moderate constipative effect on the first day, followed by attainment of the new level of bulk stools only at the third day."

In addition to its demonstrated effectiveness, L.A. Formula is unsurpassed for patient acceptance. The ulcer or colitis patient, the gravida, the nursing mother, the aged and bedridden, children, your most fastidious patient—all find improved L.A. Formula pleasant and easy to take.

We encourage you to write for samples for clinical comparison

Supplied: 7 and 14 oz. cans.

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1. Cass, L. J., and Wolf, L. P.: Gastroenterology *20*:149 (Jan.), 1952.
2. Berberian, D. A., Pauly, R. J., and Tainter, M. L.: Gastroenterology *20*:143 (Jan.), 1952.

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